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ANNUAL REPORT
OF
THE BOARD OF DIRECTORS TO THE COUNCIL
OF
THE OAK RIDGE INSTITUTE OF NUCLEAR STUDIES, INC.

June 30, 1947

The first meeting of the Board of Directors of the Oak Ridge Institute of Nuclear Studies, Inc., was held in Oak Ridge on February 14 and 15, 1947. This meeting marked the transfer of the management of the Institute from the Executive Committee to the Board of Directors according to the action taken by the Council at its October, 1946 meeting.

The meeting was attended by the President, Frank P. Graham, who served as Chairman, and by the following members: Jesse W. Beams, Ernest W. Goodpasture, Paul M. Gross, George B. Pegram, William G. Pollard and Frederick Seitz. Paul McDaniel was also present in an advisory capacity.

A draft of a contract which had been prepared by the Manhattan District was rejected as unworthy of the extensive program for which the Institute was designed. The desirability of having the Commission give great thought to the suitability of arrangements for the administration of CEW research facilities in such a way as to insure the development on a stable basis of an outstanding National Laboratory devoted to high level education of research scientists and vigorous support of fundamental reserach was emphasized.

A committee appointed by the Chairman, composed of Dr. Gross as Chairman and Dr. Goodpasture and Dr. Pegram, drew up a statement "Sphere of Activity and Objectives of the Oak Ridge Institute of Nuclear Studies" which was submitted to and adopted by the Board. Copy of this statement was sent to the Council members in March of this year. Immediately following the Board meeting, Dr. Pollard worked with the research and legal divisions of AEC here at Oak Ridge on the preparation of a draft of a letter contract based on the statement referred to above. Mr. Walter J. Williams, Director of Field Operations of AEC and Mr. A. V. Petersen assisted in the development of this draft and Mr. Williams personally brought it to the attention of Mr. Carroll Wilson in Washington on February 22. Ten days later Dr. Graham and Dr. Pollard met in Washington to complete the negotiations of this Letter Contract. Dr. Pollard spent the period March 5-7 with the legal department of the the Commission and discussed the Institute's programs and objectives at length with members of this department and also with Dr. Fisk and briefly, with Dr. Bacher. Dr. Graham had an opportunity to speak informally about the program with Mr. Lilienthal and Mr. Waymack.

A revised draft, United States Atomic Energy Commission Letter Contract No. AT-40-1-GEN-33, dated March 18, 1947 and prepared in Washington as a result of these discussions, was signed by Mr. Williams on March 21 as Contracting Officer for the Commission and by Dr. Graham on March 23 for the Institute.

MEMBERSHIP OF BOARD OF DIRECTORS AND OFFICERS

Of the members of the Board of Directors initially elected by the Council at its first meeting in Oak Ridge on October 17,1946, Dr. G. W. Beadle and Dr. M. Tuve had declined to serve and Mr. David Lilienthal had accepted, but later on November 11, 1946 tendered his resignation by letter. The President invited Dr. Jesse W. Beams to serve as alternate to Dr. Tuve and Dr. E. N. Harvey as alternate to Dr. Beadle. The terms of office of these members in accordance with Article IV, section 2 of the by-laws were determined by a drawing conducted at the meeting and the result was as follows:

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For three year terms expiring June 30, 1949:

Dr. Ernest W. Goodpasture, Dean of School of Medicine, Vanderbilt
Dr. Jesse W. Beams, Professor of Physics, University of Virginia.
Dr. George B. Pegram, Dean of Graduate Division, Columbia University

For two year terms expiring June 30, 1948:

Dr. Paul M. Gross, Professor of Chemistry, Duke University
Dr. William G. Pollard, Professor of Physics, University of Tennessee
Dr. Frederick Seitz, Director of Training School, Clinton Labs. and Chairman of the Department of Physics, Carnegie Institute of Technology.

For one year terms expiring June 30, 1947:

Dr. E. Newton Harvey, Professor of Biology, Princeton University
The poistion left vacant by Mr. David E. Lilienthal.

Dr. Harvey resigned in May and the resulting two vacant positions were not filled by the Board but were left to the annual Council meeting for regular elections.

The Board elected Dr. Seitz as Vice President and Dr. Pollard as Treasurer until June 30, 1947. The Treasurer's bond was fixed at $50,000 and has been secured.

A nominating panel was appointed from whose nominations an Executive Director will be selected. This nominating panel consists of :

Eugene P. Wigner, Chairman
Lee A. DuBridge
Arthur H. Compton
J. R. Oppenheimer
Farrington Daniels

Dr. W. G. Pollard was appointed Acting Executive Director until the permanent Director could be selected. The University of Tennessee granted Dr. Pollard a leave of absence from January 1, 1947 until September 1, 1947 to permit him to serve in this capacity.

Shortly after the Letter Contract was signed the Atomic Energy Commission provided the Institute with office space in the Adminstration Building at Oak Ridge.

The period from March 23 to April 15 was devoted to details of organization. Payments of university fees were requested and letters were written to members of the Council reporting on the Board meeting. Dr. Graham wrote the University Presidents at the same time. During this period a number of people were interviewed for positions of Administrative Assistant to the Acting Executive Director and of General Secretary. Mr. J. W. Mumford was finally selected for the former position and employed on April 17. Miss Barbara McClannahan was selected for the latter and employed on April 28.

Mr. Mumford has a B.Sc. degree in Business Administration from the University of Nebraska, has a wide and varied experience in accounting and administration, and has come to us from the position of Chief Contract Termination Auditor with Tennessee Eastman Corporation, Oak Ridge. Miss McClannahan also came to us from Tennessee Eastman Corporation.

The time since April 15 has been occupied in establishing business and administrative procedures and in getting programs, authorized by the Letter Contract formulated in detail and put into operation. During this period the main contract negotiations between the Atomic Energy Commission and the Monsanto Chemical Company for the operation of Clinton Laboratories have been carried on. As a result of the uncertainty of the scientific staff about the outcome of these negotiations it became urgently desirable for the Institute to put the case for a national laboratory at Oak Ridge before the Commission. To this end, Dr. Graham and Dr. Pollard succeeded in getting an appointment with Dr. Fisk in Washington for Monday, May 5. They obtained a firm statement from him to the effect that a basic research program, on the present scale as a minimum, would be carried on at Clinton Laboratories and that the new operating contract must make provision for this. Dr. Fisk also indicated that the Commission expected the Institute to play an ever increasing role in the operations at Clinton Laboratories, but that the detailed arrangements could be worked out only after the basis for the new operating contract had been established. Dr. Graham and Dr. Pollard both felt that this conference was most satisfactory.

The Monsanto Chemical Company accounced publicly on May 29 that it would not renew its present contract with the Atomic Energy Commission for the operation of Clinton Laboratories. As a result, the relationship of the Institute to the Clinton Laboratories cannot now be established, and the program which the Institute has submitted to the Commission for approval under its Letter Contract cannot be acted upon until a new operating contractor is selected.

The posibility of the operation of this facility by the Institute was studied and discussed at a special meeting of the Board of Directors which was called for the purpose by Dr. Graham and was held in Oak Ridge on June 14. This meeting was attended by all members of the Board. In addition three advisors who had been invited to attend by Dr. Graham, John P. Ferris and Floyd Reeves of TVA, and E. P. Wigner, Director of Research at Clinton Laboratories, were present throughout the meeting and participated fully in all discussions and concurred in the actions taken. The meeting was adjourned two hours for lunch but was otherwise in session from 9:30 A.M. to 7:00 P.M.

Material dealing with Clinton Laboratories operations was presented and discussed at the meeting. Requirements for such operations were carefully studied in some detail from the point of view of the various ways in which the Institute might assume responsibility for the conduct of a part or of all of these operations through a contract with the Atomic Energy Commission.

As a result of these considerations, those present at the meeting were able to reach complete agreement on the following findings:

(a) That the operation of Clinton Laboratories had been recognized as an ultimate objective of the Oak Ridge Institute of Nuclear Studies by the Oak Ridge Conference of December, 1945 at which it was formed: that this objective is recorded in the minutes of that conference; and that this objective was reaffirmed in February, 1947 by the Board of Directors of the Corporation in its statement to the Atomic Energy Commission entitled "Sphere of Activity and Objectives of the Oak Ridge Institute of Nuclear Studies."

(b) That now that the Atomic Energy Commission is no longer committed to the present industrial contractor for the continued operation of Clinton Laboratories, consideration by the Institute of the steps which it should take for the early attainment of this ultimate objective is necessary and proper.

(c) That, subject to certain changes in the structure and composition of its Board of Directors, operation of Clinton Laboratories by the Institute is feasible and practicable and that such a course is in accordance with the responsibility assumed by like associations of universities in other regions for the operation of similar AEC Laboratories.

On the basis of these findings, it was unanimously resolved that the Board of Directors of the Institute shall seek a contract with the Atomic Energy Commission for the opeartion of Clinton Laboratories. Other resolutions were passed recommending to the Council the adoption of amendments to the by-laws to provide for a Board of Directors of such composition and stability as would be appropriate for the adminstration of such a contract. The Atomic Energy Commission has been informed of these findings and actions.

STATUS OF INSTITUTE PROGRAM

Among other things the Letter Contract between the Institute and the Commission directs the Institute to do all things necessary to accomplish the following programs:

(a) To establish an administrative organization of the Institute at Oak Ridge, Tennessee, and to administer and accomplish a program, evidenced in writing, mutually agreed upon by the Institute and the Commission, pursuant to which selected graduate students from cooperating institutions can complete thesis research for the degree of Doctor of Philosophy, through employment with Contractors at the Clinton Engineer Works, Oak Ridge, Tennessee.

(b) To establish a program with Contractors, as approved by the Commission, pursuant to which staff members and research workers of cooperating institutions can arrange to participate, either at the Clinton Engineer Works or at their own institutions, in the research programs of said Contractors.

(c) To conduct, in and with facilities to be provided by the Commission, at Oak Ridge, Tennessee, special training programs, approved by the Commission and designed to provide scientific workers with training and experience in the special techniques of research relating to the research programs of the Commission.

In order to accomplish this directive, steps have been taken to develop the general types of activity specified in it in the form of detailed programs with appropriate budgetary provisions which, if approved by the Atomic Energy Commission, could be carried out under this contract.

The status of each of these programs is discussed under the appropriate heading in the following.

a. Graduate Training Program

This program was conceived at the beginning of the movement for the formation of the Institute at the Knoxville Conference of December 5, 1945 and the Oak Ridge Conference of December 28-29, 1945. In addition to the primary objective of securing a National Laboratory in Oak Ridge devoted to basic research and graduate education, these conferences were devoted to an extensive study of the potentialities of Oak Ridge for advanced training at the last year doctorate and post doctorate levels. Another important area of discussion centered around the "immediate needs" for the provision of opportunities for graduate courses and a complete doctorate program at Oak Ridge in order to retain in Oak Ridge Laboratories capable young scientists whose education had been interrupted by the war. The Conference was urgently requested by the Manhattan District and the operating contractors to sponsor such a program and make the necessary provisions for carrying it out. At the request of the Conference, the University of Tennessee agreed to do whatever it could to conduct such a graduate program at Oak Ridge as a branch of its Graduate School. The representatives of other universities agreed to loan to the University of Tennessee any of their faculty capable of giving graduate courses who could possibly be spared in order to assist in meeting the heavy demands imposed by this program.

With these early considerations as a background, the Graduate Training Program of the Institute has slowly evolved. A number of early proposals have been studied by scientific personnel at Oak Ridge, by Manhattan District and, later, Atomic Energy Commission personnel, and by the faculties of member universities. Out of these studies many features have been clarified and perfected and the general character of a workable and satisfactory plan has emerged. This plan has now been prepared in the form of a Memorandum of Understanding, Part I (the second part will provide for the program under b below) which, in accordance with the provisions of our Letter Contract with the Commission, is to be accepted by the Oak Ridge operating contractors and the Institute and finally approved by the Atomic Energy Commission. A copy of this Memorandum of Understanding in its present form is attached to this report as Appendix I. It is believed that essential agreement on it has now been reached by all parties, and that final negotiation of the agreement may be expected soon.

The program established by this Memorandum of Understanding is in two distinct parts according to the distinction established at the original conferences. The first part is covered by sections 1 through 13 in the Memorandum of Understanding and established the procedure by which the research facilities at Oak Ridge can be employed for Ph. D. thesis research by any university which agrees to participate in the program.

The second part is established in section 14 of the Memorandum of Understanding and consists in placing the "immediate needs" program of the original conference on an appropriate and satisfactory basis. Since that conference, the University of Tennessee has been conducting graduate courses at night and on Saturdays in available rooms in the Oak Ridge High School. Although the teaching has been done by regular members of the graduate faculty with the rank of Associate Professor or Professor as a part or, in most cases, all of their regular teaching load, the makeshift character of the facilities, the lack of library, faculty offices, student conferences, and graduate seminars has prevented the program from supplying an adequate graduate school experience for the students enrolled in it.

In January 1947 the University of Tennessee requested through President Graham the assistance of the Institute in securing adequate facilities in Oak Ridge for the conduct of this program. This request was approved by the Board of Directors at its first meeting in February. As a result this program has been incorporated as a part of the Graduate Training Program of the Institute and provisions for housing and conducting it in a suitable and adequate fashion have been included as a part of the Institute's total requirement for a building and facilities in the program which it has submitted to the Atomic Energy Commission.

If these facilities are provided by the Commission, it will be possible for the Institute to conduct at Oak Ridge through the University of Tennessee a full graduate program which will provide most of the atmosphere and indirect benefits of on-campus graduate programs in universities. This will, of course, prove of great benefit to Oak Ridge laboratories in the rentention of capable young scientific personnel and in the full development of the capabilities of such personnel.

b. Research Participation Program

The arrangements for cooperation in research between universities and Oak Ridge laboratories authorized under paragraph 1 b of our Contract with the Commission have not been studied or developed to an extent comparable with those of the Graduate Training Program. A number of arrangements of this type have, however, been handled informally by the Institute and a preliminary draft of an overall program to establish the mechanics of such arrangements has been prepared. A copy of this preliminary draft is attached to this report as Appendix II. After extensive study and revision it is proposed that this program be established in the form of a Memorandum of Understanding, Part II.

A number of arrangements of this type have been or are being serviced by the Institute on an informal basis. Among them are the following.

Arrangements have been completed to have Dr. Francis K. Talbott of the Catholic University spend this summer doing research in the Physics Division of Clinton Laboratories through temporary employment by Monsanto Chemical Company.

Arrangements were made partly through the Institute on behalf of Dr. Newton Underwood of Vanderbilt University for interviews with several departments at Oak Ridge concerning employment during a one year leave of absence from Vanderbilt. Dr. Underwood, will do research in the K-25 laboratories as an employee of Carbide and Carbon Chemicals Corporation for one year beginning September 1, 1947.

Similar arrangements were initiated for Professor Robert L. Allen of Georgia School of Technology for employment in Oak Ridge this summer. An interview was arranged for Mr. Allen with the Power Pile Division of Clinton Laboratories. However, this interview occured on the day on which Monsanto announced its withdrawal and it was not possible as a result to complete the desired arrangements for him.

A proposal for a sub-contract with Clinton Laboratories for a research program on beta ray spectra at Vanderbilt University was submitted with the Institute's recommendation to the Atomic Energy Commission. Although approved in principle by the Commission, action on it is being withheld until Clinton Laboratories operations have been transferred to the future contractor.

A proposal for a sub-contract or research participation contract with Clinton Laboratories for research programs on element 43 and on the perparation of carbon 14 labeled organic compounds in the University of Tennessee Chemistry Department is similarly being withheld until this contract transfer has been accomplished.

Like action has been taken on a request for assistance by the Institute in the negotiation of a Clinton Laboratories sub-contract for cyclotron research at the University of Illinois. In this case assistance has also been rendered in preliminary steps for the eventual purchase of tritium gas from the Commission.

Finally eight requests from students in universities or colleges of the region for assistance in finding employment in Oak Ridge Laboratories have been handled by the Institute. Several have already resulted in such employment.

c. Isotope Tracer Technique School

One of the possible special training programs authorized by this section of the Letter Contract which may be conducted by the Institute is a School in Radioisotope TracerTechniques. Such a school was considered and authorized by the Board of Directors at its first meeting. A detailed proposal for this program was submitted with the rest of our contract program to the Atomic Energy Commission. A copy of this proposal is attached to this report as Appendix III. This plan was developed in response to a large number of requests for this type of service which the Institute had received. A detailed budget for equipment, staff, and materials together with building space requirements was included in the program submitted to the Commission.

BUSINESS AND ADMINISTRATIVE MATTERS

The Board decided at its first meeting to request half of the annual contribution of $5,000 to cover the period January 1 to June 30, 1947 from each of the fourteen member universities. Twelve of them have made the requested payment of $2,500 so that $30,000 has been received to date.

An audit has been made of the funds of the Executive Committee, and the Treasurer has refunded the balance ($557.50) to the original contributors. A report to all contributors and delegates to the December 27--29 Oak Ridge Conference is being prepared. When this is completed the Executive Committee will be dissolved.

All accounting systems and procedures necessary to the conduct of the business of the Institute and the securing of reimbursement under the AEC Letter Contract with the Commission have been put into operation.

Compensations of the Administrative Assistant and the General Secretary are reimbursable under the contract. Office supplies, when possible, are requisitioned directly from AEC stocks. Office expense, postage, and travel expense as authorized by the Contracting Officer are reimbursed by AEC under the Contract.

Public Liability (coverage $50,000 per person and $100,000 per accident) and Workmen's Compensation (coverage $10,000 per person) policies have been secured.

A financial statement is attached to the report covering the period ending June 30, 1947.

VANDERBILT ISOTOPE SYMPOSIUM

As authorized by the Board at its first meeting, the Institute was co-sponsor with Clinton Laboratories of a five-day symposium on clinical and tracer uses of radioisotopes which was conducted by Vanderbilt University April 21-25, at the Medical School in Nashville. There were eighty-six registrants including the speakers at this symposium. It has been widely acclaimed as highly successful affair.

RELATIONSHIP WITH THE TENNESSEE VALLEY AUTHORITY

The TVA was represented on the Executive Committee and participated actively in much of its work. The Proposal for the formation of the Institute which was submitted to the Manhattan District in August 1946 was based to a very large extent on a draft prepared by TVA. Moreover, the TVA provided all of the legal assistance required by the Executive Committee in the preparation of proposals, the Charter of Incorporation, by-laws and contract drafts.

With the dissolution of the Executive Committee, the TVA lost its representation in the Institute and it became desirable to seek some other way to maintain contacts between the two organizations. To this end the Board at its first meeting resolved that it would look with favor on entering into a contract with the Tennessee Valley Authority for advisory and consultative service to the Institute.

On the basis of this action the problem was investigated and it was found that no strictly contractual agreements were involved but that a formal document defining and establishing the areas of mutual interest and assistance between the two organization was desirable. In order to accomplish this end, the Institute and the TVA cooperated in the preparation of a draft of a Memorandum of Understanding between the two parties. This draft was read to the Board at its second meeting and was approved for final negotiation by President Graham and the TVA. Final execution of this Memorandum of Understanding is expected soon.

APPENDIX I

MEMORANDUM OF UNDERSTANDING, PART I

MEMORANDUM OF UNDERSTANDING, PART I

BETWEEN

THE OAK RIDGE INSTITUTE OF NUCLEAR STUDIES

AND

THE MONSANTO CHEMICAL COMPANY (For Clinton Laboratories)

AND

THE CARBIDE AND CARBON CHEMICALS CORPORATION
(For K-25 and Y-12)

This Memorandum of Understanding, Part I, is made and entered into this First day of July, 1947, for the purpose of establishing a Graduate Training Program of the Oak Ridge Institute of Nuclear Studies (hereinafter referred to as the "Institute") at Oak Ridge, Tennessee, with the object of utilizing in the doctoral training programs of existing graduate schools the unique facilities, both of equipment and staff, for graduate research and instruction in nuclear and related sciences which are available at the Clinton Engineer Works (CEW) installations being operated for the United States Atomic Energy Commission by the Monsanto Chemical Company and the Carbide and Carbon Chemicals Corporation (hereinafter referred to as "operating contractors").

1. Date of Initiation of the Program.

The Graduate Training Program set forth in this Memorandum of Understanding, including the supplementary program for regular employees of CEW contractors defined in section 14, will be put into effect for the academic year 1947-48, beginning in September, 1947.

2. Scope of the Graduate Training Program.

The program is open to any approved graduate school in the United States, which grants the Ph. D. or equivalent degree in any one of the fields - Physics, Mathematics, Chemistry, Biology, and Engineering - and which agrees to participate in it on the basis set forth in the following. Such a university will be known as a "participating university."

The program is limited to the performance of thesis research leading to the Ph. D. degree and such special courses and seminars directly related to this research as may be available at CEW Laboratories or the Institute. An essential requirement for eligibility to the program is therefore the successful completion by the student at his University of the basic course requirements for the degree.

The program is not open to candidates for the Master's degree.

The program is designed for regular graduate students enrolled in participating universities and it in no way limits or affects the arrangements which have been, or are hereby made for the graduate training of regular employees of CEW contractors. Such arrangements are set forth in the supplementary agreement for such employees in section 14 of this agreement.

The Institute will grant no academic degrees in its own right.

In all matters of mutual interest to participating universities and the operating contractors, the Institute will act as liaison capacity.

3. Academic Standards

This program will be conducted and administered by a resident staff selected by the Executive Director of the Institute and approved by its Board of Directors. This staff will assist the Executive Director in the discharge of the obligations of the Institute to participating universities and CEW Laboratories for the proper conduct of the graduate study program.

The Institute assumes responsibility to participating universities for the quality of work performed in this program, for the maintenance of adequate academic standards in all aspects of graduate training at Oak Ridge, and for keeping each participating graduate school informed of all developments relevant to the granting of a degree to one of their candidates prior to approval of his program or of changes in it.

Any special or advanced courses offered directly by the Institute at Oak Ridge or given under Institute supervision by an operating contractor, or other agency, will be conducted in accordance with recognized academic standards and the Institute will arrange for the granting of graduate credit through an existing university for the successful completion of such courses.

4. Staff

The Graduate Training Program will be conducted by a resident staff consisting of (a) any staff members who may in the future be employed by, and hold academic rank in, the Institute, (b) the "Resident University Staff," and (c) the "Research Associates of the Oak Ridge Institute of Nuclear Studies."

It is anticipated that the Institute may find it necessary to employ a small graduate faculty competent to conduct more advanced phases of doctoral programs, in order to supplement the course offerings of its member institutions so that doctoral programs can be initiated in them. Members of such a faculty would carry an academic rank in the Institute and would be listed as Institute faculty in any announcement of this program.

The second group will include university faculty who have been placed on leave by their universities for employment at a CEW Laboratory, or otherwise made available to it in support of the interest of such universities in the development of this program. They will be listed separately under the heading "Resident University Staff" in any announcements of the Institute's program and the name, university as-

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sociation, and academic title of each individual will be given in such a listing.

The third group will consist of regular members of the scientific staffs of the CEW Laboratories and will be chosen in consultation with, and subject to the approval of, the Director and Division Directors of the laboratory concerned. They will be appointed to the position of Research Associate of the Institute by its Board of Directors. Initially the number of Research Associates will be small but this number will be expanded as the program develops. The Research Associates of the Institute will be listed as such in any bulletins or announcements issued by the Institute concerning this program.

5. Security

The thesis research performed under the auspices of the Institute in this program will in general be concerned only with declassified or declassifiable problems. However, the Institute is prepared to make special arrangements for classified theses when they are desired by the participating graduate school or are required by unanticipated developments in the progress of specific research projects.

In any case, the Institute will observe in all aspects of its program all applicable government security regulations. In particular, all students placed in the program, regardless of the classification of their research, must obtain the usual security clearance and this also applies to Institute or university staff members directly involved in supervising or assisting such students at CEW Laboratories.

6. Institute Fellowships

Students who are candidates for doctoral degrees in participating universities and are employed by a CEW Contractor for the purpose of performing their thesis research under the auspices of the Institute will be known as "Graduate Fellows of the Oak Ridge Institute of Nuclear Studies". They will be employed by the Contractor as "Student Employees" to distinguish them from regular employees.

The minimum number of Institute Fellowships available for this program for 1947-48, will be sixteen at the Clinton Laboratories (five in physics, three in chemistry, five in biology, and three in engineering), and the corresponding minimum numbers at K-25 and Y-12 will be five each. The operating contractors agree to make provision for a least these numbers of student employees unless circumstances beyond their control prevent them from doing so.

Student employees will receive compensation from the company employing them at the rate of $230.00 per month initially and will be subject to normal salary increases at the end of the first year. The classification of "Student Employee" and the salary range associated with it will be subject to approval by the Atomic Energy Commission.

Traveling expenses of student employees and of their families, if any, covering travel to Oak Ridge incident to their becoming employed and return at the termination of their employment will be paid by the Contractor under the standard arrangement used by the Company in such cases.

Any regular employees who are participating in the special graduate program set forth in Section 14 of this Memorandum of the Understanding will, upon successful completion of qualifying examinations for the Ph.D. degree, be permitted to participate fully in the program described here for Institute Fellows except that

(1) the procedure for application and selection set forth here in sections 7 and 8 will not apply to them, and

(2) their regular Company salary will not be affected or altered as a result of the salary fixed above for student employees.

7. Application for Institute Fellowships.

Application for Institute Fellowships will be made only by the Dean of the Graduate School of a participating university on printed forms provided for the purpose by the Executive Director. Such applications will be made on behalf of candidates for the Ph.D. degree in the Graduate School of which he is the Dean for students in physics, chemistry, biology, mathematics, or engineering who have completed, or who he expects will successfully complete all formal course requirements for the degree prior to the date set for filling the fellowship for which application is being made.

8. Selection of Institute Fellows.

The Executive Director of the Institute will appoint a "Committee on Admissions" for Clinton Laboratories and a similar committee for K-25 and Y-12 combined.

At least half of the membership of each committee will consist of Research Associates from the laboratory concerned and the remainder will consist of Research Associates from other laboratories when security clearances permit and of Resident University Staff and Institute Faculty associated with the laboratory concerned. The Executive Director will be an ex officio member of each committee.

The Executive Director will submit all applications which he has received to the appropriate committee whenever any openings for Institute Fellowships are to be filled. The Committee on Admissions will review the applications and select from them those which it approves for acceptance. This selection will be made on the basis of scholastic achievement and research ability, the needs of the research program of the CEW Laboratory involved, and considerations of service to the widest possible group of universities. If the committee desires to approve more applicants than the number of existing vacancies permit, it may ask the Director of Research of the laboratory involved to meet with it to discuss the possibility or advisability of making special arrangements for additional Fellowships in that laboratory.

After this selection has been made, the applications approved by the Committee on Admissions are transmitted by the Executive Director to the Director of Research of the Laboratory involved. Subject to his approval of the applicants, he will submit them to his employment office with a formal request for the employment of the individual applicants as student employees. All negotiations concerning their employment will be carried on entirely between the employment office and the individuals concerned in the usual way. If for any reason, such as failure of security clearance, a candidate is not employed, another approved applicant may be selected and submitted for employment in the manner outlined above. The employment office will keep the Executive Director informed on the status of these negotiations so that suitable action may be taken by him in informing the various Graduate Deans of the status of their applications.

9. Nature of Graduate Study Program

The Institute Fellows will have no regular duties at the CEW Laboratory in which they are employed beyond those involved in the performance of their thesis research, but in all other respects these student employees will be subject to the same rules, regulations, and restrictions as regular employees of the Contractor.

The selection of research problems for Institute Fellows will be made on the basis of the general policy of confining this program to research requiring the special or unique facilities at CEW for its performance. Such problems must be consistent with the approved resesearch program of the Contractor involved. As previously indicated problems will in general be chosen from declassified or declassifiable portions of the research program.

The Executive Director will appoint certain members of the Institute Staff to meet with him in a conference with each new Institute Fellow and his Division Director or Supervisor for the purpose of making this selection of a suitable research problem.

After satisfactory selection of a research problem has been made for an Institute Fellow, the Executive Director will appoint, with the advice and consent of the Director of the Division to which the Fellow has been assigned, a Graduate Committee of three members. This Committee will advise the Fellow on his research and graduate study while in Oak Ridge, be responsible to the Institute and to his Graduate School for the quality of his work, and will constitute a portion of his examining body at the termination of his Fellowship. The Chairman of this Committee will be a resident staff member of the Institute as defined in Section 4 hereof. The second member need not be an Institute staff member, but must be a permanent staff member of the laboratory and be closely associated with the direction of the research performed by the Fellow.

The third member will be named by the Dean of the Graduate School in which the Fellow is enrolled and will in general be a member of the graduate faculty of that school.

Institute Fellows will be expected to attend their Division Seminars and such other special seminars or Training School courses as their grad-

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...ate committee may direct, subject to any fixed limitations on such activities as may prevail in the particular laboratory concerned, and to the requirement that attendance at such seminars and courses shall in no case reduce the time devoted to the performance of their assigned research below a minimum of thirty-six hours per week.

10. Examinations

On completion of his research at Oak Ridge, each Institute Fellow will be required to take an oral or oral and written examination on his thesis research and related background material and allied subject matter.

This examination will constitute the basis for recommending the acceptance of the student's thesis by the graduate school granting the degree. Such recommendations will be formulated by the examining body after the examination and transmitted to the Dean of the Graduate School in writing by the Executive Director.

The examining body will be the Fellow's Graduate Committee as described in the preceding section plus one additional faculty member named by the Dean and one additional Institute staff member from the laboratory concerned. Any Institute staff member or staff members of the University may attend and participate fully in these examinations. Others may attend only by invitation of the Executive Director. The university granting the degree will be expected to send those of its faculty who are members of the student's examining body to Oak Ridge for this examination. When requested to do so by the university, the Institute will endeavor to reimburse the university for a part or all of the traveling expenses incurred by its members in attending such examinations.

These examinations will, in general, be non-classified and will cover only declassified or unclassified material. In special cases of classified theses, these examinations will, of course, be calssified also. In these cases faculty members from the institution granting the degree can participate in the examination only if the usual security clearance can be obtained for them and other applicable security measures are met. The Executive Director will assist the participating universities in meeting these requirements in such cases.

It is considered to be a vital element in the success of this program to have the participating universities and graduate schools substitute this examination at Oak Ridge for the usual final examination at the university. In view of the opportunity which each university has in this program to examine its students on all matters except the thesis prior to their appointment as Institute Fellows, such an arrangement does not appear to be unreasonable. It is hoped that universities participating in the program will find it possible to modify their doctorate requirements to the small extent necessary to conform with this procedure.

11. Publication

Any research completed by an Institute Fellow at a CEW Laboratory will first be written up and issued, subject to the approval of the Director of the Laboratory, as a project report of that Laboratory in

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the usual manner for research contributions from Atomic Energy Commission Laboratories.

Such reports, when unclassified or declassified, may be submitted in whole or in part for publication in any appropriate scientific journal or other outlet if the university with which the student is affiliated approves. Such publications will show the affiliation of the student as:

__________University,__________, and Clinton Laboratories, Oak Ridge, Tenn.,

__________University,__________, and K-25 Laboratory, Oak Ridge, Tenn.,

__________University,__________, and Y-12 Laboratory, Oak Ridge, Tenn.,

together with a footnote explaining that the work was performed while the author was a Graduate Fellow of the Oak Ridge Institute of Nuclear Studies and that the ________Laboratory is operated for the United States Atomic Energy Commission by________________Company.

Such reports may also be submitted, either as such or in revised form, as a thesis in partial fulfillment of the requirements of the university with which the student is affiliated for the degree of Doctor of Philosophy. The Institute will cooperate with the university to insure that its special requirements for the form or character of Ph. D. theses are met in the material submitted to it by an Institute Fellow.

Classified theses may be accepted on behalf of the University by the candidate's examining body, provided all members of this body have obtained security clearance from the Atomic Energy Commission. Copies of such classified theses may be deposited with the Institute as custodian during such period as they remain classified or they may be deposited under seal with the University if it has approved facilities for handling classified material.

12. Announcements

As already indicated, the Institute will issue a printed announcement describing the program as soon as this Memorandum of Understanding has been executed by the parties involved. This announcement will be circulated to all graduate schools which offer doctoral programs in one or more of the fields of interest.

In addition to information on resident staff, procedures for application and admission, description of the Fellowships, examination procedures, etc., this announcement will contain a description of opportunities for research and graduate study in the various fields which are offered at Clinton Engineer Works. The Directors of the various Divisions and Laboratories will assist in the preparation of non-classified material suitable for this purpose.

This announcement will also urge each graduate school to notify the Institute as far in advance as possible of its intention to make application for an Institute Fellowship for a given student in order that the Institute can arrange for correspondence or a conference between the Oak Ridge Laboratory and the University Department concerned for advice

13. Tenure of Fellowships

Institute Fellowships will be granted only for periods of one year subject to renewal at the end of the first year.

At the end of the first year the record and achievement of each Institute Fellow will be reviewed by his Graduate Committee which will recommend the renewal or termination of his Fellowship. Fellowships will be renewed by the Executive Director of the Institute with the approval of the Director of the laboratory. If renewal is not justified, the Director of the laboratory concerned may at his discretion either initiate termination procedures for the student or transfer him from the status of student employee to that of regular employee.

Recommendation to the company for wage increases for Fellows whose appointments are renewed for the second year will be initiated by the Division Director concerned after consultation with the Fellow's Graduate Committee.

In general, each Fellow should plan on two years for the completion of his thesis research. In exceptional cases in which more time is required, the Fellowship may be renewed for a third year but in no case will the tenure of a Fellowship exceed three years.

14. Supplementary Agreement for Regular Employees of Operating Contractors

The Graduate Training Program set forth in the foregoing establishes arrangements for doctorate work which are primarily applicable to university students who are not now employed by an operating contractor. The purpose of this supplementary agreement is to establish arrangements through which regular employees of the contractors can complete the requirements for the Ph. D. degree through the graduate training facilities of the Institute in Oak Ridge, without terminating their employment with the contractor.

A. Employees Who Have Not Completed A Major Portion of the Course Requirements for the Ph.D. Degree

Regular employees of an operating contractor who wish to undertake a program of study leading to the Ph.D. degree in physics, chemistry, mathematics, or biology, or to the Master's degree in engineering can do so through an arrangement which the Institute has made with the University of Tennessee.

The necessary courses will be offered by the University of Tennessee in Oak Ridge, conducted by regular members of the university's graduate faculty and will carry standard residence graduate credit. The courses will be conducted in a suitable building in Oak Ridge to be supplied to the Institute by the Atomic Energy Commission and adequately equipped with class room, laboratory, and library facilities.

To be eligible for the program an employee must obtain the approval of his employer and must be acceptable to the University of Tennessee. The approval of the employer will be transmitted in writing to the Executive Director of the Institute prior to the date for course registration set by the University. No students will be registered for courses under the program unless such approval has been obtained for them. After this registration the Institute will supply each employer with a list of his employees registered by the University in this program and of the course load for which each employee registered.

Students registering for one course of three credit hours may be required to reduce their normal work week from 40 to 36 hours with an attendant reduction in their salary to 90% of the nominal amount. Classes will be scheduled for them on Tuesday and Saturday mornings (or such times as may be mutually agreed upon by the parties to this Memorandum of Understanding). They will be excused from work for four hours on Tuesday morning (or such other time as may be agreed upon above).

Students registering for two courses of six credit hours will, in general, be required to reduce their normal work week from 40 to 30 hours with an attendant reduction in their salary to 75% of the nominal amount. Classes will be scheduled for them on Monday and Friday mornings as well as on Tuesday and Saturday mornings (or such other times as may be mutually agreed upon by the parties to this Memorandum of Understanding). They will be excused from work for four hours on Tuesday morning and for three hours on Monday and Friday mornings (or such other times as may be agreed upon above).

No student may register for more than six credit hours at any one time while in the employ of an operating contractor.

It is expected of students taking graduate course work in this program that they maintain an average grade of B or better for all courses and that they will have passed their preliminary examinations not later than three years from the date of their admission to the program.

Each student whose graduate work in this program has been satisfactory will, three months prior to the date scheduled for his preliminary examination for the doctorate be granted a leave of absence of three months by the Company employing him. During this period he will devote himself to full time study in preparation for his examinations.

Class schedules, registration fees, grade reports, and similar matters will be determined by the University of Tennessee. Students may apply to the University for Graduate Assistantships carrying remission of fees during the period of part time employment and for Graduate Fellowships providing financial assistance in the three month period during which they are on leave from their Company.

Students who have successfully passed their preliminary examinations will automatically become eligible for the programs set forth in subsection B below. Upon successful completion of the remainder of their studies under this program, the University of Tennessee will grant them the degree for which they have been working.

B. Employees who have completed all, or nearly all, of the formal course requirements for the Ph.D. degree.

Any employee who has, prior to his employment, completed all formal course requirements for the Ph. D. degree may, with the approval of his employing Company, make arrangements with his university to complete his thesis research and other requirements for the degree through the organization and plan outlined in the preceding sections for Institute Fellows.

Such arrangements do not involve application and selection for an Institute Fellowship (as in sections 7 and 8) but require only that the Dean of the Graduate School of the University involved agree to the completion of the requirements for the degree through the organization and plan set up in the foregoing for Institute Fellows. The compensation for such employees may be arranged by their employer without regard to the salary agreed upon for Institute Fellows.

Employees who have completed nearly all of the course requirements for their degree may, with the approval of their employer, arrange with their university to take the remainder at Oak Ridge with the University of Tennessee. They will then be permitted to take a three month leave of absence to return to their university for the purpose of taking their preliminary examinations.

IN WITNESS WHEREOF, the parties have caused this Memorandum of Understanding to be executed by their authorized representatives as of the day and year first above written, and approved for each of them by the Atomic Energy Commission.

Attest: OAK RIDGE INSTITUTE OF NUCLEAR STUDIES, INC.

_______________ BY_______________

Acting Secretary President

Attest: MONSANTO CHEMICAL COMPANY

_______________ BY_______________

(Title) (Title)

Attest: CARBIDE & CARBON CHEMICAL CORPORATION

_______________ BY_______________

(Title) (Title)

1026572

Approved ______________ ______, 1947

UNITED STATES ATOMIC ENERGY COMMISSION

____
(Title)

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APPENDIX II

PROPOSED RESEARCH PARTICIPATION PROGRAM

PROPOSED RESEARCH PARTICIPATION PROGRAM

[illegible] THE OAK RIDGE INSTITUTE OF NUCLEAR STUDIES, INC.

[illegible] purpose of the Research Participation Program of the Oak Ridge [illegible] of Nuclear Studies is to establish arrangements through which [illegible] members and research workers in universities and other research and [illegible] institutions can participate, either at the Clinton Engineer [illegible] (CEW) or at their own institutions, in the research and development [illegible] of the operating contractors at CEW.

Except in the case of arrangements for direct contracts or agreements [illegible] such a university or institutions and the United States Atomic Energy [illegible] (AEC), which the Institute will confine to the Commission's re- [illegible] the program will be open to any qualified university or other re- [illegible] or development institution in the United States without geographical [illegible] regional limitations.

[illegible] aspect of the proposed program is the formulation of detailed [illegible] for placing university staff members and other research workers [illegible] appropriate staff position in a CEW laboratory through temporary full [illegible] employment by the operating contractor involved. This aspect is set [illegible] in detail in Section A of this proposal.

The other aspect of the proposed program is the formulation of detailed [illegible] for contractual or other agreements between an operating con- [illegible] and a university or other institution, or an individual connected [illegible] such an institution, whose purpose is to provide a formal basis for [illegible] participation. This aspect is described in Section B of this Pro- [illegible]

SECTION A

Employment of University Staff by Operating Contractors

The operating Contractors agree to refer to the Institute all requests [illegible] they may receive from a university or from their own scientific staff [illegible] divisions for the employment for a limited period of one year or less of [illegible] university staff member or other research worker who would be placed on [illegible] of absence by his university or other institution during the period [illegible] such employment.

The Institute agrees on its part to assist the operating contractors [illegible] every way open to it in locating suitable personnel for positions which [illegible] desire to fill on this basis.

The Institute will prepare a printed application form for this portion [illegible] its program which will make provision for all information required by [illegible] of the operating contractors in their own application forms for re- [illegible] or development positions, and will also provide for such additional [illegible] information as the Institute may require. The period of time for which the individual concerned will be granted leave by his institution and the nature of the research or other work which he is interested in performing would be given. The application would provide for a statement of the applicant's willingness to take research assignments in the regular research programs of the operating contractor or, alternatively, a description of the particular research problem for the performance of which the applicant desires employment at CEW and access to specialized research facilities.

The Institute will submit to prospective applicants the usual Personnel Security Questionnaire and related forms, together with the above application form. When these forms are completed and returned, the Institute will, if it approves the applicant and wishes to recommend his employment, submit the PSQs and related forms directly to the Security Division of the AEC in order to initiate clearance procedures as rapidly as possible.

The Institute will review the application and formulate its recommendations in writing. It will then submit copies of the application and of its recommendations to appropriate research or development departments of CEW according to the following table:

Field of Intrest of Applicant	K-25 Research	K-25 Technical	Y-12 Research	X-10 Physics	X-10 Chemistry	X-10 Biology	X-10 Technical	X-10 Power Pile	X-10 Training School	X-10 Health Physics	
Mathematics	X	X	X	X			X		X	X	
Engineering	X	X	X				X	X	X		
Physics	X		X	X		X			X	X	
Physical or Inorganic Chemistry	X		X		X	X	X	X	X		
Organic Chemistry	X		X		X	X			X		
Biology						X				X	

The Division or Department Head of each of the departments receiving such material will notify the Institute within four days of its receipt by them concerning their interest in taking further steps leading toward the possible employment of the applicant. Those departments who wish to

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give the employment of the applicant further consideration will notify the Institute of the nature of the positions for which he would be considered including the nature of the research opportunities involved.

The Institute will then write the applicant and describe in a general and, of course, unclassified way the available openings at CEW for the period which he specifies. The applicant will be requested to indicate those positions in which he is interested and to set a date for a trip to Oak Ridge for interviews which the Institute will arrange with the departments concerned.

When a final selection, agreeable to the applicant and to the department, has been made, the regular company application form will be completed either by the Institute or the Company from the information given in the Institute application, and when completed will be signed by applicant. Further negotiations concerning employment will be conducted entirely between the applicant and the company. When they have been completed, the employer will notify the Security Division of the AEC of such employment according to a procedure to be fixed by the latter.

Compensation for such positions will be fixed for an individual on leave from a university at a monthly rate equal to one-ninth of the annual salary which he received from his university for the regular academic year unless the amount so determined exceeds the approved salary range for the position involved, in which case only the maximum amount in this range will be paid.

Compensation for an individual on leave from any other research or development institution or concern will be fixed at a monthly rate equal to one-twelfth of his annual salary unless the amount so determined exceeds the approved salary range for the position involved, in which case only the maximum amount in this range will be paid.

Arrangements for reimbursement for travel to Oak Ridge at the beginning of employment and for return at its termination need not be standardized but can be determined by the employing company in each individual case.

Individuals placed on limited term employment with an operating contractor through this program will be wholly responsible to the contractor and will have no obligations to the Institute beyond those mutually agreed upon for Research Associates of the Institute in Part I of the Memorandum of Understanding.

However, publication of research completed by such staff members will show the joint affiliation of the author with his university or other institution and with the laboratory in which the work was performed according to the plan adopted for Institute Fellows in Part I of the Memorandum of Understanding.

SECTION B

Formal Agreements for Research Participation

In order to facilitate the integration of basic research activities in universities and other institutions with those conducted at CEW, it is proposed that two kinds of formal agreements of a contractual nature be employed. The first kind will be the usual sub-contract or Consultant Contract already in use by CEW contractors. It will continue to be employed as in the past for the purpose of carrying out obligations undertaken by an operating company in its prime contract with the Atomic Energy Commission.

The second type is new and is proposed here as a means of serving research participation between CEW laboratories and universities or other institutions on a cooperative basis and with the objective of establishing the mutual interest of both parties to the agreement in the attainment of common goals. The provisions proposed for this type of agreement are set forth in detail later in this section.

In either case, the function of the Institute will be to discover potentialities for such research participation, render assistance to universities or other institutions or to CEW contractors in the formulation of detailed proposals for such arrangements when such assistance is requested by the organization concerned, and in such cases to submit recommendations to the other party on the basis of such proposals. In no case will the Institute be a party to the contracts or other agreements arising from such proposals or recommendations and their negotiation will be conducted by the two parties to the proposed agreement without prejudice by the Institute's recommendations. However, the Institute may, at its discretion, when requested to do so by one party, act as agent for that party in these negotiations with the other.

Very little more need be specified here concerning the first type of agreement. Subcontracts and Consultant contracts will continue to be employed by CEW contractors for the purpose of arranging with other organizations or individuals for the performance or conduct of such portions of their approved programs as the organization or individual may be specially equipped to undertake for the prime contractor. These arrangements will continue to originate primarily at the instigation of the CEW contractors. Forms for such contracts, approved by the AEC, already exist and are in use by the contractors.

The other type of agreement is not, however, in general use at present. If the present proposal is adopted, an essential element in its adoption will be the development by the operating contractors of detailed forms for contractual instruments suitable for this purpose and the approval by the Atomic Energy Commission of these forms. A suggested basis for the form of such instruments is set forth in the following.

1. Character of Arrangements

Since, in general, the arrangements under consideration will involve

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little, if any, financial commitments on the part of either party to them, the instrument supporting them could well be titled an "Agreement" or a "Memorandum of Understanding" rather than a "Sub-contract".

2. Recital Clauses for Research Participation Agreements.

The following form for the recital clauses to be employed in these research participation agreements is suggestive only but should serve to clarify the basis and intent of the arrangements which are being proposed:

"WHEREAS, ______________ Company (a CEW operating contractor) has entered into a contract with the United States Atomic Energy Commission, dated __________ (Contract No. ________), hereinafter called the "principal contract", under which Contractor, agreed to do all things necessary to continue the operation of the ______________ (description of CEW facility) at Oak Ridge, Tennessee, known as ______________ (name of CEW facility), and to perform research and development services, and

"WHEREAS, Contractor finds it necessary in the conduct of such operations and the performance of such research and development services to conduct investigations and perform research in ____

(description of contractor's research or development program in which participation is to be effected), and

"WHEREAS, ______________ University (or other institution or individual) through its departments of ______________, is conducting similar investigations and performing related research in ____

(description of university's research or development program in which participation is to be effected), and

"WHEREAS, the parties believe it would be to their mutual advantage and of assistance in the proper discharge of their respective obligations in the conduct of these investigations and the performance of these researches to enter into the cooperative arrangements hereinafter set forth:

"NOW THEREFORE in consideration of the premises and of the mutual covenants herein contained, the parties agree as follows:"

3. Performance Clauses and Provisions

Detailed provisions for performance under these agreements would of course vary widely among individual agreements but they should all, in general, make provision for the following matters:

a. The university personnel to be involved in the cooperative research arrangements should be individually named and appropriate provision for FBI clearance of such individuals should be made.

b. Provisions for exchange of information and reports should be set forth in detail including all necessary security provisions for classified formation and reports and for their proper handling by the university.

c. In the matter of publication, provision should be made for review by either party, prior to issuance or submission for publication of reports or papers prepared by the other party bearing on the subject of the agreement. Topics for separate publication and those for joint publication by both parties should be defined in the agreement or, in lieu of such definition, procedures for determining how results are to be reported or published should be established.

d. Provision should be made for the loan of special equipment, materials, or services, by either party to the other for the purpose of facilitating the research covered by the agreement. These provisions could define the term of such loans, the manner of return, and the responsibility for damage.

e. Provision should be made for conferences and consultation between staff members of both parties - either at the CEW Laboratory or the university or institution involved. Arrangements for reimbursement to either party for travel and subsistence expense in connection with attendance at such conferences should also be established.

f. When necessary, provisions should be included for the performance by specified members of the university staff at CEW of those portions of the research which require access to or use of fixed CEW facilities.

g. Any financial commitments by either party to the other which are required or justified by the nature of the research program or by inequities in the extent of the services required of one party over those required of the other would, of course, also be established in the agreement. In general, it is expected that such commitments will be small or non-existent for this type of agreement. However, most of them should make provision for reimbursement for travel and subsistence expenses to individuals when engaged in business necessary to carrying out the provisions of the agreement.

SECTION C

Other Contractual Arrangements

In some cases, the Institute may find, after investigation and study of proposals submitted by a university or other institution, that the proposed program could more properly be supported directly through a contract with the Atomic Energy Commission or some other agency such as the National Science Foundation. In such cases, the Institute reserves the right to submit the proposal with its recommendations to the Commission or other agency provided the institution making the proposal agrees to this course.

APPENDIX III

PROPOSED TRAINING SCHOOL
IN
RADIOISOTOPE TECHNIQUES

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THE OAK RIDGE INSTITUTE OF NUCLEAR STUDIES, INC.

PROPOSED TRAINING SCHOOL IN RADIOISOTOPE TECHNIQUES

1. Purpose

This special training program is intended as a service to university and industrial laboratories, agricultural experiment stations, medical schools, and other organizations who desire to employ labeled atom techniques in their research programs but do not at present have available the personnel or equipment for such work. The objective of the program will be to develop familiarity with the use of radioactive isotopes as a technique and research tool in tracer studies. It is not the purpose of the training program to develop an understanding of various research problems which have been or could be solved by means of this technique. Neither is it anticipated that the program will produce fully trained technicians in the use of radioactive isotopes.

2. Application and Admission

The program will be widely advertisied throughout the United States by means of announcements sent to universities, industries, medical schools, etc., and through announcements submitted to scientific and technical journals.

Selection of applications will be made on the basis of previous training and experience of the individual applicants and the evidence submitted of the intent of the institution which they represent to establish a laboratory for isotope tracer work. A secondary but important consideration in this selection will be to insure that the training program renders the widest possible service both geographically and by type of institution or research activity.

Trainees will pay a registration fee of $25.00 for the program and will also defray their own traveling expenses, subsistence and lodging while in Oak Ridge for the program. Only dormitory or hotel space will be available for trainees.

Selection of applicants will be made by a committee of three consisting of the Executive Director of the Institute, the Chief of the Isotopes Branch of the Commission and the Director of Isotope Tracer School.

3. Administration and Organization

The school will be held in a suitable centrally located building in Oak Ridge supplied by the Commission. This building will be equipped with suitable class rooms, laboratory, library, and office space. The apparatus, materials, and supplies needed for instruction will also be supplied by the Commission.

All requisitions for apparatus, materials, and supplies will be

[redacted]

submitted by the Director of the School and approved by the Executive Director of the Institute and the Contracting Officer assigned to the Institute by the Commission. The Contracting Officer will determine for each of these requisitions whether it is to be filled by (a) Institute purchase order reimbursed by the Commission, (b) loan from another Commission contractor such as Clinton Laboratories, or (c) from surplus Commission or government stocks.

The maximum number of trainees which can be accomodated is forty eight.

The term of the school will be determined by its Director but will be about four weeks. The starting date will be determined by the Director of the School, the Executive Director of the Institute, and the Chief of the Isotopes Branch of the Commission so as to allow a sufficient period for necessary preparations and at the same time best suit the convenience of the trainees who will be expected to attend.

The instructional staff for the school will be chosen by the Director. Staff members who are employed at the time by other Commission contradtors will, with the approval of such contractors, be made available to the Institute without compensation by it for specified times during a specified period mutually agreed upon by the Contractor and the Institute. Other staff members will be employed by the Institute on a basis approved in advance for reimbursement by the Commission for which the following is suggested:

(a) Traveling expenses plus subsistence during travel to and from Oak Ridge.

(b) Compensation by single payment for the six week period commencing one week prior to the opening date for the school and ending on week after the closing date.

The Director of the School will be employed for a period of between three and four months commencing at least two months before the opening date for it.

4. Description of Training Program

The instructional program will be divided about equally between laboratory and lecture. Lecture courses will be scheduled between 9:00 A.M. and 12:00 noon on Monday, Wednesday and Friday. Special lectures and seminars will be scheduled occasionally on Monday or Friday afternoons. The remainder of the time on Monday and Friday afternoons will be devoted to informal conferences between the instructors and the trainees and to demonstrations of equipment by commerical manufacturers.

The laboratory will be conducted partly by demonstration and partly by direct performance of experiments by individual trainees. The demonstration laboratory will be scheduled for the entire group on Wednesday afternoon from 1:30 P.M. to 4:30 P.M. The individual laboratory work will be conducted in smaller sections with a maximum of twelve trainees per section. The entire group will be divided into four equal sections for this purpose. Two of these sections will meet from 8:30 to 11:30 on Tuesday and Thursday mornings in two separate rooms under separate instructors but performing the same experiments. The other two sections will meet in the same way from 1:30 to 4:30 on Tuesday and Thursday afternoons.

The lectures on Monday and Wednesday mornings from 11:00 to 12:00 will be devoted to a discussion of the laboratory work to be performed on the following day. The remainder of the lecture time will be assigned in appropriate amounts to the following topics.

(1) Basic Physics: Neutrons, protons, and nuclei. The alpha, negative beta, positive beta, and K capture types of radioactive transformations. Rules of nuclear stability and charts of nuclei. Scattering, absorption, and dection of beta and gamma radiations. Law of radioactive decay, decay constant, half life, etc. Nuclear isomers. Units-roentgen, curie, etc.

(2) Instruments: Ionization chambers, Geiger-Mueller counter tubes, preamplifiers, scaling circuits, cathode ray oscilloscopes, counting rate meters, electroscopes amd electrometers, photographic detection. Analysis for stable isotopes—mass spectrograph.

(3) Design of tracer experiments: General principles and examples of successful experiments in microbiology, medicine, plant physiology, zoology, metallurgy, etc.

(4) Radiochemistry and techniques: Tracer-carrier relations and techniques for quantitative determinations of tracer amounts. Errors from scattering and absorption. Preparation of samples for counting. Special problems with low energy beta emitters like C^{14}.

(5) Design of small Radioisotope Tracer Laboratory: Principles in design of such a laboratory. Location of hoods, design of radiation barriers, special tools, forceps, etc. Monitoring procedures. Useful special equipment. Procedures for waste collection, concentration and disposal.

(6) Health Physics and precautions: Nature of radiation damage. Radiation monitoring and warning systems. Precautions required in handling radioactive materials. Prevention of laboratory contamination. Disposal of radioactive wastes. Calculation of tolerance amounts or rates of intake for various isotopes.

(7) Production of Isotopes and Sources: Cyclotron produced isotopes. Pile produced isotopes. Separated stable isotopes.

(8) Procurement of Isotopes and Equipment: Commerically available instruments. Characteristics, cost, delivery, etc. Procedures for application for isotopes. Available isotopes and cost.

(9) Related Seminars: These would consist of special lectures on radiation effects on gene mutations, chromosome breads, and

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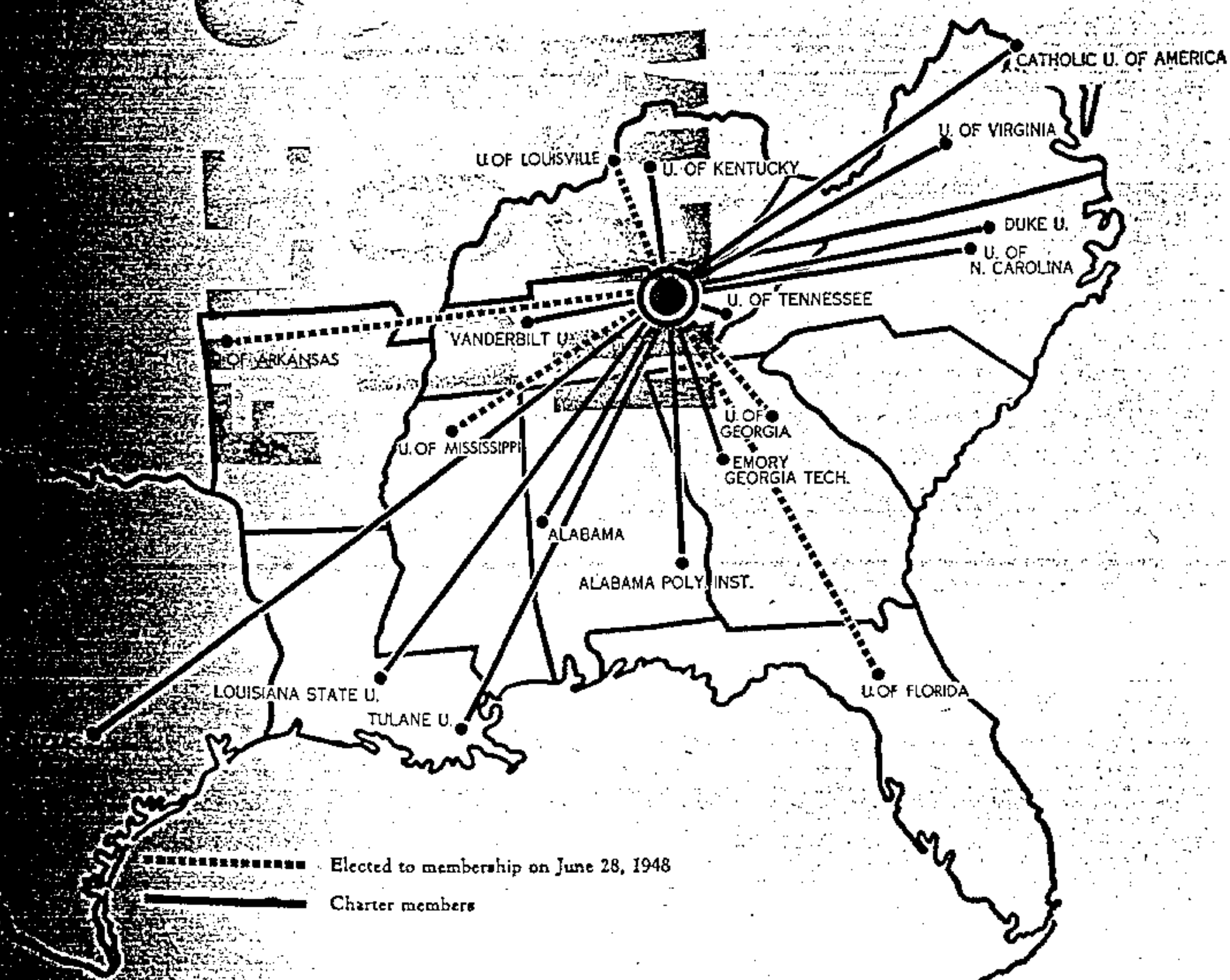
OAK RIDGE INSTITUTE OF NUCLEAR STUDIES

INCORPORATED

ANNUAL REPORT 1947 - 1948



OAK RIDGE, TENNESSEE

SECOND ANNUAL REPORT
OF
THE BOARD OF DIRECTORS TO THE COUNCIL
OF
THE OAK RIDGE INSTITUTE OF NUCLEAR STUDIES, INC.

June 30, 1948

INTRODUCTION

The Oak Ridge Institute of Nuclear Studies rounds out its second full ar with its major training programs launched and an enduring foundation id for a broad program of service. As the year draws to a close, there ems every reason for confidence in the future of the Institute in service its sponsoring universities, the Atomic Energy Commission, and the Nation a whole.

The past year has been a difficult one for the Institute. During this iod all the varied problems of creating and establishing a new organiz- ion have had to be faced and solved. These problems include assembly of aff; development of suitable personnel policies and employee benefits; tablishment of adequate accounting, purchasing, property record, and other fice procedures; the solution of many legal problems of corporate lia- ility and responsibility including the determination of adequate insurance erage and types of insurance needed; together with many others incident establishing a going organization. Those problems are by no means all lved at the present stage but great progress has been made during the year coping with many of them.

In addition to those problems peculiar to the management and functions our corporation itself, our energies have been absorbed from time to e with the several major crises arising during the year in the management program of the Oak Ridge National Laboratory (formerly Clinton Labora- ies) as described in detail in the first section of this report. Since welfare and stature of this Laboratory constitutes the primary concern the Institute, it was essential that we forego the development of our organization and programs during each such crisis in order to lend our ll support to the Laboratory. This situation has naturally multiplied problems greatly and slowed our progress considerably.

In spite of this very difficult period, the Institute is in a far strong- position than ever before. This statement is based on several factors. is the fact that the Commission has recognized the Institute as an in- al part of Oak Ridge and a key element in its plans for developing the Ridge Area on a lasting and permanent basis deeply rooted in this region. s are the very earnest desire on the part of the Carbide Company to op- e X-10 as a true national laboratory, their complete cooperation with Institute in organizing its programs, the strong possibility of obtain- important new research projects at Oak Ridge National Laboratory, and very warm support accorded the Institute by Mr. J. C. Franklin, Manager Oak Ridge Directed Operations, and of his representative Dr. H. M. Roth administers the Institute contract with the Commission.

It is in the field of relations with its member universities that the ress of the Institute has been slowest during the year. This has been tly due to the several changes in management of Oak Ridge National Lab- tory which have necessitated a new start each time in negotiations on suit- plans for participation in the laboratory by university staff members graduate students, and partly it has been due to the great pressure of problems demanding immediate attention in connection with establishing our corporation and launching its contract with the Commission. With many of these initial problems out of the way, we are looking forward to a period of greatly increased service to our member universities during the coming year.

In conclusion we can say that nothing has changed the fact that Oak Ridge contains research and training facilities unmatched in the world, and failure to utilize these facilities for the advancement of science would be an educational disaster of the first order. The Institute is now recognized by all concerned as the proper agency--and the only agency--which can fulfill the high promise inherent in Oak Ridge.

SECTION I. CLINTON NATIONAL LABORATORY NEGOTIATIONS

Changes in Contract Operator At Clinton National Laboratory

On the last day of the 1946-47 fiscal year, the Institute Council by resolution asked the Atomic Energy Commission to meet with the Board of Directors to discuss the operation of Clinton National Laboratory by the Institute and thereby fill the vacuum in management that had resulted from the withdrawal of the Monsanto Chemical Company from Oak Ridge. The Council also approved appropriate changes in the Institute's by-laws and in the composition of its Board to meet the larger responsibilities that would necessarily devolve on the Institute should it be named to operate Clinton National Laboratory.

Following the Council meeting in June, a telegram and follow-up letter were sent to Mr. Lilienthal transmitting the Council's resolution requesting a meeting of the Board of Directors with the Commission for consideration of a contract with the Institute for the operation of Clinton Laboratory. Shortly after this, a letter was received from Mr. Carroll Wilson in response to a letter which Dr. Pollard had sent to Dr. Bacher prior to the Council meeting. This letter from Mr. Wilson stated that the Commission felt that it was necessary for it to choose an operating contractor with established management experience, construction experience, and a large reservoir of experienced management and technical personnel. He said that although the Commission felt that full participation by the Institute in the Clinton National Laboratory was essential, they did not feel that a meeting with the Board was desirable at that time.

Negotiations by the Commission with several possible industrial contractors to assume the operating role at Clinton Laboratory were unsuccessful, and the Commission approached the University of Chicago around the middle of July with a view to exploring the possibility that it might take over the contract for this operation. Officials of the University agreed to explore the possibilities, but insisted that they should first determine the attitude of the Institute and of the Laboratory staff. A series of meetings were held in Oak Ridge for this purpose on August 12 and 13.

In the meantime, Dr. Graham called Mr. Lilienthal on August 8, and on finding that the Commission Chairman was away from Washington, he talked to Mr. Waymack instead. In this conversation, Dr. Graham emphasized the importance to the Commission of developing and strengthening, rather than weakening, the regional university concept represented by the Institute. It was agreed that neither the Commission nor the University of Chicago would proceed further with contract negotiations unless it was completely satisfactory to the Institute.

On August 12, five representatives of the Commission and five from the University of Chicago came to Oak Ridge for the purpose of carrying out initial exploratory discussions with the Institute and with scientific staff members of the Laboratory. Dr. Pollard met with the group on the morning of the 12th and later the entire group went to Clinton Laboratories and met during the afternoon with a number of representatives of the Laboratory staff.

On the next day, August 13, Dr. Pollard met with the Commission representatives alone and at this time it was agreed that the meeting between the Board of Directors and the Commission which had been requested at the time of the Council meeting should be held. This meeting took place on the following day, August 14, in the Atomic Energy Commission building in Washington. Present at the meeting were Board Members Graham, Beams, Gross, Pegram and Pollard for the Institute and Messrs. Wilson, Fisk, Huddleson, Marks, and McDaniel for the Commission. (Board Members Goodpasture, Painter, Seitz and Wigner were unable to attend the meeting.)

Although several plans of operation were discussed, primary consideration was given to the two possibilities of operation by the University of Chicago on the one hand and the Oak Ridge Institute on the other.

The point of view advanced by the Board Members of the Institute was based largely on the philosophy of regional management of the Commission's national laboratories. The Institute, as the representative of the leading universities in this section, provided a strong and enduring basis for such operation. A contractor otherwise selected could not provide the same continuity of service, nor could it be deeply rooted in the hopes and aspirations of a region. Moreover, operation by the Institute had been throughly considered by the Council at its meeting on June 30, and all necessary steps had been taken by the Council to modify the organizational structure of the Institute for this purpose.

The Commission representatives brought out several points, all of which weighed considerably with the Commission in favor of the University of Chicago as contractor for this operation. The great urgency and primary importance of the reactor program on the one hand and the need for a quick return to management stability of the Laboratory of the other, both had impelled the Commission to seek a contractor with a large reservoir of scientific personnel and extensive experience in this type of operation under government contract. Two primary aspects of the problem had combined to single out the University of Chicago as the most appropriate agency for meeting these demands. On the one hand, the General Advisory Committee to the Commission had strongly recommended a consolidation of all reactor development work at one site and it further indicated that among the various possible sites the Argonne National Laboratory appeared to be the most likely. On the other hand, the University of Chicago had already served for a considerable period during the war as contract operator of Clinton Laboratories and thus could supply a background of experience for this particular operation which no other candidate would possess. The Commission felt that in placing the two laboratories in which reactor development work was being carried out, namely Argonne and Clinton, under the same management, it would be going far toward meeting the recommendation of its General Advisory Committee and it would at the same time provide an operator for Clinton of sufficient experience and resources to get operation going well at a minimum of time and thus make possible a bigger advance in the reactor development field.

After a thorough discussion of these points of view, the Institute representatives reported that its services as operator of the Laboratory were still available, but that it would cooperate fully with the University of Chicago as contract operator of the Laboratory, provided that it did not compete with the Institute's recognized academic and training functions. It was agreed that a meeting between representatives of the Institute, the Commission and the University of Chicago would be called at an early date for the purpose of working out detailed arrangements under which the objectives of the Institute could be achieved with the University of Chicago as operator of the Laboratory. The Board designated Dr. Pollard to represent it at such a meeting.

Arrangements for this meeting were made by the Commission and it was held in Washington on August 28. Dr. Pollard and Mr. Charles Snepp, Legal counsel, attended for the Institute in accordance with the action taken by the Board. Those representing the Commission at this meeting were Messrs. J. B. Fisk, S. G. English, P. W. McDaniel, H. Roth, E. E. Huddleson, Jr., and C. C. Vogel. William B. Harrell and Warren C. Johnson represented the University of Chicago. At this meeting, detailed arrangements were worked out whereby the University of Chicago would operate Clinton National Laboratory purely as a management function, with all educational and academic activities, including the Laboratory training school, managed by the Institute. It was also arranged to have the Board of Directors of the Institute act in an advisory capacity to the Director of the Laboratory with respect to the research program, budget, and policies in much the same capacity as that exercised by the Argonne Board of Governors.

The development of graduate research facilities in Southern universities in conjunction with the Laboratory was not discussed in detail, inasmuch as Dr. Fisk stated that the Commission-sponsored support for University research programs had not yet been formulated. Accordingly, this phase of the Institute's program, to the extent it contemplates such Commission-sponsored support, must await the development of Commission policy in this matter.

The terms of the proposed operating contract with the University were discussed in detail. Dr. Pollard stated that the Institute felt that it would like to consider the possibility of working toward the eventual end of assuming the responsibility for the operation and management of the Laboratories, but recognized the factors involved and the difficulties of attempting to predict when the Institute could realize this objective. Dr. Fisk stated that the Commission continued to recognize the aspirations of the Institute, but in entering into a contract with the University of Chicago for four years, the Commission felt it must maintain itself in a position to extend that term upon expiration if at that time such a course appeared desirable, and that no commitment could be made that a contract with the University would not extend beyond four years. Dr. Pollard agreed that the Institute was not asking the Commission to take a different position to that stated by Dr. Fisk.

Public announcement of the assumption of the operating role by the University of Chicago was made jointly on September 25 by the University, the Institute and the Commission. Negotiations had been completed in a most cordial manner, and the University gave every indication that it would cooperate fully with the Institute in setting up its eduational and training programs.

Immediately following the public announcements, the Institute and the University began negotiations with a view to drawing up a subcontract under which the Institute would conduct those portions of its program which utilized the Clinton Laboratory staff and facilities, and at the same time, provide for an advisory committee from the Institute to assist the laboratory staff in the scientific aspects of its program.

The Board of Directors of the Institute devoted considerable time at its fourth regular meeting on October 31 to various aspects of the negotiations. Dr. F. C. VonderLage, Acting Director of the Clinton National Laboratory Training School, and later Mr. William B. Harrell, Business Manager of the University of Chicago, met with the Board to discuss the future arrangements for this school and the relationships of the Institute with the University of Chicago. Dr. VonderLage discussed a written proposal which he had prepared for a school at the Laboratory. Mr. Harrell discussed the desire of the University of Chicago to cooperate with the Institute and reaffirmed the arrangements which had been developed for the operation of Clinton National Laboratory.

Negotiations continued satisfactorily during the period prior to January 1, 1948, on which date the University of Chicago was to take over operations from Monsanto Chemical Company. They had progressed to such a point that the Bulletin announcing the Institute's Graduate Training Program was in process of being printed and arrangements for other Institute programs were proceeding in a similarly satisfactory manner.

Appointment of Carbide as Laboratory Operator

On January 1, 1948, the Commission announced that all reactor research would be moved from Oak Ridge and be consolidated at the Argonne National Laboratory, that the University of Chicago was withdrawing from its contract to operate Clinton National Laboratory, and that Carbide and Carbon Chemicals Corporation would become the contract operator of the Laboratory.

This drastic change was of vital concern to the Institute and its member universities. Morale slipped dangerously at the Laboratory, and the move threatened the entire program of the Institute. Immediate steps were taken to clarify the situation and attempt to solve the very serious problems it raised.

The Institute had been notified of this proposed action on December 30, just in advance of similar notification in Oak Ridge to the other parties concerned. Board members were informed that night and the next day of the proposed development, and Dr. Pollard held several conferences with Commission personnel. On January 3, he attended a meeting of the laboratory staff and AEC representatives and talked with Mr. Lilienthal by telephone for more than an hour that afternoon. Other conferences and telephone calls continued until late Saturday night. There were additional conferences on Sunday, January 4, with Commission and Laboratory personnel, and a radiotelephone call that night to Dr. Graham, who was on a warship near Java, was unsuccessful for technical reasons and Dr. Graham agreed to come into Batavia to resume the conversation 24 hours later. On the evening of January 5, the entire situation was discussed in detail with Dr. Graham, with Dr. K. Z. Morgan of Clinton Laboratory participating in the conversation. As a result of this conversation Dr. Graham sent a cablegram to President Truman which emphasized

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the effect of this move on scientific progress in the South. Dr. Graham asked that a meeting of the Board of Directors be called immediately and he outlined a number of considerations which he wished to have brought before the Board on his behalf.

The Board of Directors convened at Oak Ridge late on January 6, and remained in session through January 7. The morning of January 7 was devoted to a meeting with Division Directors and other scientific personnel at the Laboratory. All members of the Board were present except President Painter and Dean Goodpasture, who were unable to attend. During the afternoon the Board met with representatives of the Commission and Carbide and Carbon Chemicals Corporation. These meetings in general resulted in an impasse, inasmuch as the Commission gave no indication of any possibility of a change in its policy, while the Board on its part could see no way to preserve the Laboratory and maintain anything approaching a National Laboratory for the South under the terms established by the Commission.

On the following day, Thursday, January 8, Dr. Pollard met with Dr. Curry of Carbide and also with Mr. Franklin of the Commission. Out of the former meeting, a statement on the part of Carbide and Carbon Chemicals Corporation of its position with respect to this operation and the extent to which the company would be in a position to cooperate with the Institute in achieving its objectives was formulated and included in a letter to the Board of Directors of the Institute. A copy of this important letter is attached to this report as Appendix I. Although this statement on the part of Carbide gave evidence of a very satisfactory viewpoint with respect to its operation of the Laboratory and held considerable promise of an extensive cooperation with the Institute in achieving its objectives at the Laboratory, a complete breakdown in negotiations between the Laboratory, the Commission, and Carbide which had been reached at this point made the hope of early progress along these lines extremely remote. It was felt that at this stage a meeting between the Board of Directors of the Institute and the Atomic Energy Commissioners themselves was essential and arrangements were made by telephone with Mr. Lilienthal that evening for holding such a meeting in Washington on the following day. The very short notice made it impossible to assemble all of the members of the Board and it was in fact not even possible to contact all of them to inform them of this meeting.

This meeting was held in Washington on the afternoon of Friday, January 9, between Board Members Beams, Gross, Pollard and Seitz and Mr. Lilienthal and Mr. Waymack, who were the only members of the Commission in the city at that time. Dr. Gross and Dr. Seitz in particular presented a very thorough analysis of the effect which this decision was having on the scientific staff of the Laboratory, the expected effect on the reactor development program, and the difficulty of achieving a national laboratory devoted to basic research of an academic type under the conditions proposed by the Commission. It was emphasized that after a thorough on-the-spot study at Oak Ridge, the Board of Directors was still of the opinion that removal of the reactor development program would be a serious blow to the Oak Ridge National Laboratory.

Mr. Lilienthal and Mr. Waymack emphasized to the Board that this step had been a working decision taken on a balance of many complex factors, among the effect of this move on scientific progress in the South. Dr. Graham asked that a meeting of the Board of Directors be called immediately and he outlined a number of considerations which he wished to have brought before the Board on his behalf.

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Mr. Lilienthal and Mr. Waymack emphasized to the Board that this step had been a working decision taken on a balance of many complex factors, among

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which could be cited the continued management instability at the Laboratory during the fall, the inability of the University of Chicago to find a suitable Research Director for the Laboratory, the impossibility of reconciling the personnel policies for the Laboratory which the University of Chicago desired to incorporate in its contract with those in effect with other operating contractors in the Oak Ridge Area, and the renewed recommendation of the General Advisory Committee that all reactor development work be consolidated at one site. A continuation of the policy to proceed with construction of the high flux reactor at X-10 along with support of a reactor development program would have involved the Commission in the commitment of a very large sum of money over the next five years. Moreover, this large expenditure would have had to have been made against the advice of the Commission's scientific advisers and placed under the control of a management whose adequacy and stability was by no means assured. They emphasized that the decision, once having been made, had to be carried through quickly and that no reconsideration of it could be contemplated at this stage. They urged instead that the Institute adopt a constructive policy and actively cooperate with the Commission and Carbide in bringing to realization the very considerable opportunity for the development of an outstanding national laboratory for the South which still remained. This point of view was subsequently set forth in a letter from Mr. Lilienthal to Dr. Graham, a copy of which is included with this report as Appendix II.

This meeting was highly satisfactory for both parties and resulted in a very clear and effective presentation of the interests and requirements of the Institute and of the essentials for good scientific laboratory management. The members of the Board who participated in it agreed that the only remaining alternative for the Institute was to cooperate actively with the Commission and the Carbide Company in making the transition to Carbide management at the Laboratory and to lend its efforts toward reconciling the scientific staff of the Laboratory toward this course. The Commission recognized with the Board the great difficulty of making such a course of action effective but welcomed the adoption of it by the Board as the only feasible alternative. Primary attention during the following few days was given to obtaining the support of the scientific staff of the Laboratory for this course of action and working out some of the details with them. Finally, Dean Gross came to Oak Ridge on Tuesday evening, January 13, and on Wednesday he and Dr. Pollard met with the Division Directors of the Laboratory. At this meeting it was decided that the Institute should recommend to Carbide and the Commission that Dr. Frederick Seitz be made Director of the Laboratory. A number of other research facilities and modifications of the Laboratory research program were also agreed upon to take the place of the research program which had been planned in connection with the high flux reactor and agreement was reached with respect to general personnel policies which Carbide should be requested to adopt for this operation but which did not include some of the policies over which objection had been previously raised. By Thursday, January 15, the Laboratory staff and the Institute were essentially in agreement on a plan for operation of the Laboratory under Carbide management which appeared very hopeful indeed. On this day Dr. Fisk and Dr. Bacher of the Commission and Dr. Felbeck of Carbide all came to Oak Ridge and a meeting was held between Dr. Fisk, Dr. Bacher and Dr. Pollard early Thursday afternoon. The only element of this plan discussed at that

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time was the selection of Dr. Seitz as Research Director of the Laboratory. Both Commission representatives enthusiastically concurred in this choice and suggested that it be discussed with representatives of Carbide as soon as possible. Arrangements were therefore made immediately for a meeting between Dr. Pollard for the Institute and Dr. Felbeck, Mr. Center and Mr. Rucker for Carbide. This meeting was held late thursday afternoon and resulted in calling Dr. Seitz and asking him to come to Oak Ridge by plane that night. On the following day, Friday, January 16, Dr. Seitz spent the morning and a portion of the afternoon in conference with representatives of Carbide. The result of these discussions was that Dr. Seitz found the conditions advanced by Carbide Company completely satisfactory and was in complete agreement with their plan for operation of the Laboratory. He informed them of his willingness to accept the appointment subject to a clarification of the Commission's plans for the research program to be carried out at the Laboratory. He met with Dr. Fisk and Dr. Bacher during the afternoon and evening of the same day for this purpose but was unable to obtain assurances which he regarded as adequate with respect to the possibility of filling the vacuum left by removal of reactor design activities and the building of the high flux reactor.

On the following morning, Dr. Seitz and Dr. Pollard met again with the Laboratory Division Directors. Dr. Seitz reviewed the discussions of the preceding day and the considerations which were uppermost in his mind with regard to his acceptance of this appointment. He reaffirmed his great confidence in the Carbide Company and their willingness and ability to achieve successful operation of X-10 as a National Laboratory and he expressed his belief that the arrangements which had been developed with Carbide showed great promise of meeting all the problems which he led the Commission initially to make this decision. He emphasized that he felt it would not be possible for him to successfully direct the work of the Laboratory and exercise effective leadership of its scientific staff unless some rallying point could be provided in the scientific program to take the place previously occupied by the reactor development program and the high flux reactor.

Following this meeting, Dr. Seitz returned to Pittsburgh and negotiations were continued by telephone during the next three days. None of the ensuing discussions led to a resolution of the difficulties which had been encountered and Dr. Seitz finally decided against the acceptance of his appointment to this position.

At the time of their meeting in Washington with Mr. Lilienthal and Mr. Waymack, Dr. Pollard, Dr. Gross and Dr. Seitz had had dinner with Dr. Gibson, Acting Director of Applied Physics Laboratory in Silver Springs, Maryland, and had tentatively discussed with him the possibility of his being interested in the position of Research Director at Oak Ridge National Laboratory.* After some

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*Clinton National Laboratory was redesignated as Oak Ridge National Laboratory in January, 1948, by the Atomic Energy Commission. Since the name Clinton Engineer Works had been abandoned in favor of Oak Ridge Area the former name was no longer appropriate.

deliberation, Dr. Gibson was next recommended to the Carbide Company for consideration as Director of the Laboratory. But at the request of the Commission the Institute did not in this case take an active part in negotiations with Dr. Gibson which followed his nomination. These negotiations were quite prolonged but finally proved unsuccessful inasmuch as Dr. Gibson was later offered and accepted an appointment as permanent director of the Applied Physics Laboratory.

On March 1, 1948, Carbide took over the operation of the Laboratory from Monsanto Chemical Company with Mr. C. N. Rucker of the Carbide Company in the position of Executive Director. The sympathetic understanding with which Mr. Rucker has dealt with the problems of the scientific staff of the Laboratory, the vigor with which he has pushed the scientific program developed by the Division Directors and the interest he has shown in developing compromises between industrial procedures and the management requirements of a scientific Laboratory have all contributed greatly to the welfare of the Laboratory during this difficult period. The management of the Laboratory has been most cooperative in assisting the Institute in making suitable arrangements at the Laboratory for university staff members and graduate students and extensive programs of this type are anticipated for the future.

The first half of the year 1948 has been an exceedingly difficult one for the Laboratory. The loss of the high flux reactor and the entire reactor development program has been a very serious blow, and the resultant shock to the morale of the scientific staff has resulted in a rather heavy loss of valuable personnel at the Laboratory. Coming on top of this blow a strike threat delayed by Federal injunction and ending finally in a compromise on June 13, added greatly to the problem of achieving a stable situation at the Laboratory. In spite of these difficulties, however, the Commission is prepared and anxious to support a strong National Laboratory in Oak Ridge, and both the Institute and the Carbide Company are determined to achieve this end regardless of the difficulties in the way. Nothing that has happened has altered the fact that the Oak Ridge National Laboratory possesses research facilities and opportunities unparalleled anywhere else in the world, that life in the city of Oak Ridge holds much that is attractive to scientific personnel, and that all of the elements of an outstanding scientific laboratory still exist here. Given competent and enthusiastic scientific leadership and a return to management stability, such a Laboratory can be achieved. These elements both the Institute and the Carbide Company are determined to supply at the earliest possible date.

SECTION II. INSTITUTE PROGRAMS

Graduate Training Program

The Graduate Training Program of the Institute was described at some length in the annual report of last year. At that time, this program was incorporated in a Memorandum of Understanding between the Monsanto Chemical Company, the Carbide and Carbon Chemicals Corporation and the Institute, which was ready for execution in May, 1947. Final execution of this agreement was, however, prevented by the decision of the Monsanto Chemical Company not to renew its contract for the operation of Clinton Laboratories. Pending the selection of a new contractor during the summer of 1947, this program was held in abeyance. In the fall of that year negotiations were resumed with the University of Chicago on this and other programs of the Institute. Rapid progress in these negotiations was made and complete agreement was reached by December, 1947, on all aspects of the program. At this time, a Bulletin and Announcement of the Graduate Training Program was prepared and sent to the printer to be issued around the the first of the year but the order for printing was canceled as soon as it was learned that the University of Chicago would withdraw from its contract to operate the Laboratories and that Carbide and Carbon Chemicals Corporation would be the new operator.

During January, the energies of the Institute were absorbed in problems connected with this change, but soon thereafter the entire Bulletin and Announcement was extensively revised in accordance with the new arrangement and negotiations were resumed with the Carbide Company. These were successfully completed in March and the Bulletin was finally published in April and distributed to all graduate schools in the country as well as to interested industrial organizations and other agencies. The Institute is now beginning to receive applications on behalf of candidates for Fellowships and it is expected that several may be filled by September, 1948. The first graduate Fellow of the Institute reported to the Biology Division of the Oak Ridge National Laboratory on May 3, to begin his thesis research. He is Mr. Leighton A. Nutting, a biology major in the Graduate Division of the Virginia Polytechnic Institute. He is pursuing research on the fermentation of some non-hexose sugars, for his Ph.D. thesis under the supervision of Dr. Stanley Carson and Dr. Paul Tompkins, both Research Associates of the Institute and Dr. Fred S. Orcutt, Professor of Biology at the Virginia Polytechnic Institute. The Institute is now engaged in perfecting arrangements under which Dr. Orcutt can be brought to the Oak Ridge Laboratory at freqent intervals to confer with the other two members of Mr. Nutting's Graduate Committee and participate actively in the research which Mr. Nutting is carrying on. The Institute hopes that it can develop such arrangements quite generally for all of its Fellows.

Arrangements have been completed to expedite the flow of information between the Institute Graduate Committee and the Fellow's University Committee. Communications between the two groups will be cleared by a responsible staff reviewer at the Laboratory involved, and no additional clearance will be necessary unless the communcation contains restricted information. This does not apply, of course, to research reports or theses which students may eventually prepare for submission to their universities. Such full reports or theses will be submitted for declassification in the usual manner.

The Committee on Admissions held an organizational meeting on May 28, 1948 and set up four appropriate sub-committee to review applications for Fellowships in the major fields of Biology, Chemistry, Engineering and Physics. Dr. A. Dixon Callihan was named chairman of the Committee. The composition of the Committee on Admissions is as follows:

Oak Ridge National Laboratory

Dr. William A. Arnold	Dr. Karl Z. Morgan
Dr. Stanley F. Carson	Dr. Morris E. Rose
Harold Etherington	Dr. William L. Russell
Dr. William A. Johnson	Dr. John A. Swartout
Dr. Henri A. Levy	Dr. Fred VonderLage
Dr. Stuart McLain	Dr. Earnest O. Wollan

K-25 Laboratory

Dr. A. Dixon Callihan	Dr. George A. Garrett
Dr. James L. Gabbard	

Y-12 Laboratory

Dr. Christopher P. Keim	Dr. Robert S. Livingston

It was agreed that the Executive Director of the Institute would direct applications for Fellowships to the Chairman of the Committee on Admissions who would then route them to the appropriate sub-committee. Each member of the sub-committee will review the qualifications of the applicant and note that he should be: 1) accepted, 2) rejected, 3) considered by another sub-committee since his training borders two or more fields.

An indication of the acceptability of an applicant will be accompanied by a statement from the Committee member concerning the availability, in his area, of facilities for undertaking the desired research problem. It is anticipated that in such cases the application will have been considered by the Laboratory Director and other members of the appropriate Division. The application, after circulation to all members of the sub-committee, will be returned to the Chairman of the Committee with all pertinent comments. The Chairman may call a meeting of the sub-committee to determine final action.

In the course of the meeting, it was suggested that each application be considered as though several had been submitted from which a choice was to be made. This was intended to preclude the automatic acceptance of all early applications.

All members of the Committee on Admissions are Research Associates of the Institute.

It should be pointed out here that the staff of Research Associates selected for work with the Fellows is of outstanding calibre, and without exception, they are anxious to cooperate fully with the Institute in this important program. The quality of work turned out by the Fellows should be very high.

This program has been and will continue to be one of central features of the Institute. If successful, it will make a major contribution to graduate training in universities throughout the country by making otherwise unobtainable special research facilities available to all of them on an equal footing.

Research Participation

The heart of the National Laboratory idea is to be found in provisions for extensive opportunities for special research and advanced study at the Laboratory by university scientific staff members, students who have just completed their doctorate training, industrial research workers, and others who can contribute to the research programs of the Laboratory and at the same time acquire new knowledge, facility in new research techniques, and a familiarity with research problems of interest to the Commission to the lasting benefit of both the Commission and the country. This basic point of view has apparently found wide acceptance among representatives of the Commission, its contractors, and the scientific world in general. The problem of making the facilities of the Oak Ridge National Laboratory accessible to Southern university people is being approached along three independent lines as discussed below.

One approach to which the Commission is giving serious consideration and careful study is that of delineating certain portions of its research activities which can be declared completely unclassified and freed from security controls in the publication of research results. If such unclassified fields of research can be established, it will contribute greatly to solving the problem of university participation in the research programs. If, in addition to arrangements for removing restrictions on publication of results in these fields, the laboratories in which such research is conducted could be isolated from those in which classified work is done, the accessibility of such laboratories to university people would be greatly increased. The Board of Directors strongly supports this course of action on the part of the Commission, and the following resolution was adopted at the October 31 meeting:

> "RESOLVED, that the Board of Directors of the Oak Ridge Institute of Nuclear Studies strongly approves and supports the efforts being made by the Atomic Energy Commission to delineate and establish unclassified fields or areas of research; that an early and effective application of this policy to research laboratories in the Oak Ridge Area would greatly accelerate the attainment of the objectives of the Institute; and that, specifically, the Board strongly urges on the Commission the desirability of an early removal of security restrictions on the facilities and program of the Biology Division of Clinton National Laboratory in the Y-12 area."

The Institute is pushing this matter as actively as possible with the Commission and is giving support and assistance to its efforts in this direction whenever possible. One very important step along this line which the Commission has recently taken is that of announcing its intention to remove all security restrictions from the city of Oak Ridge. This will be of great value to the Institute since all of our facilities are located in it. One of the strongest reasons which led the Commission to take this step was the value to the Institute of removing as many barriers as possible between its central programs and the region which it serves.

A second approach to the problem of making the laboratories more accessible to the universities is that of arranging for Council members and a number of other staff members of the sponsoring universities to be cleared for access to Oak Ridge Laboratories. These clearances are intended to admit university staff members to the laboratories to become familiar with new fields of research and new techniques and to use the laboratory facilities here for carrying out their own research problems; to work with graduate students from their university who have been placed in the laboratory through the Graduate Training Program; and to attend special seminars, symposia, and programs of advanced study at Oak Ridge National Laboratory.

Various types of arrangements are available under which university staff members may accomplish these ends, and the Institute is prepared to assist the universities in determining the most feasible arrangement to consider in each case. The Institute will act in a liaison capacity between the Laboratory and the University in completing the desired arrangement. Among the arrangements which have been in standard use are employment for limited periods of three months or longer during off quarters or semesters on leave-of absence status, consultant contracts on a token basis, and short non-recurring visits to the Laboratory without formal employment or contracts.

Steps are being taken to name these staff members of the universities as consultants to the Institute rather than to the Laboratory directly. This procedure permits the staff member to be reimbursed for traveling expenses to and from the Laboratory. A sub-contract or working agreement will have to be worked out with Carbide to make the Laboratories accessible to these consultants.

The clearance procedure is necessarily involved. It takes from three to three and a half months to complete the process, and efforts to reduce this time have not been successful to date. However, at the present time 9 individuals from member universities have been cleared for access to the laboratories here, and clearance procedures have initiated on 21 others for whom clearance has not yet been granted.

The number of university staff members beginning work on research projects in Oak Ridge Laboratories this summer is most encouraging in view of the rather difficult year just concluded by the laboratories and the Institute. Nine of the member universities are represented at the laboratories this summer. Individuals participating in the research projects are as follows:

Oak Ridge National Laboratory

Dr. Reuben A. Day, Associate Professor of Chemistry at Emory University;

Dr. Rose Mooney, Professor and Head of the Department of Physics at Sophie Newcomb College;

Dr. Arthur S. Rowe, Associate Professor of Chemistry at the University of North Carolina;

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[redacted]

Dr. Eric Rodgers, Professor and Head of the Department of Physics at the University of Alabama; and

Dr. Wilbur A. Selle, Professor of Physiology at the University of Texas Medical School.

K-25 Laboratory

Dr. Richard C. Keen, Professor of Physics at Louisiana State University.

Y-12 Laboratory

Dr. Douglas A. Hill, Associate Professor of Chemistry at Duke University.

Dr. Day will spend the summer and fall in the Laboratories here, and the remainder will report to their universities at the beginning of the fall term of school. In addition to this group, Dr. Newton Underwood, of Vanderbilt University, spent the 1947-48 school year with the Biology Division of Oak Ridge National Laboratory, and Dr. Albert Brauer, Professor of Zoology at the University of Kentucky, reported to the Biology Division in July for a six-months' period of research. Dr. Ray G. Noggle, of the University of Virginia, will spend a year with the Biology Division beginning February 1, 1949. Considerable negotiations were conducted with a view to placing Dr. H. P. Riley, of the University of Kentucky in the Biology Division of Oak Ridge National Laboratory and Dr. William M. Breazeale, of the University of Virginia, in the K-25 Laboratory, but in both cases it was decided to defer these arrangements until a later date.

A third line of approach to making this a true National Laboratory is one of making arrangements under which outstanding scientists in the Oak Ridge Laboratories may be sent to Southern Universities to give lectures on scientific subjects at departmental seminars, Sigma Xi meetings, or general evening meetings of scientific groups. The presence of the outstanding staff available at Oak Ridge represents a scientific resource that should be drawn upon to the greatest extent possible. The Institute has been granted budgetary provisions to pay the traveling expenses of these lecturers.

Among scientific staff members in Oak Ridge who gave lectures before various groups during the year are:

Dr. Alexander Hollaender, Director of the Biology Division of Oak Ridge National Laboratory, addressed the annual meeting of the Alabama State Medical Association in Mobile;

Dr. Pollard addressed Sigma Xi meetings at the University of Kentucky and North Carolina State College;

Dr. Alvin Weinberg of the Physics Division of Oak Ridge National Laboratory spoke at a reactor colloquium at Durham sponsored jointly by Duke University and the University of North Carolina;

Dr. Ralph T. Overman, Acting Head of the Department of Special Training of the Institute, addressed the meeting of Memphis Section of the American Chemical Society at the University of Mississippi.

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The Radioisotope Program

The initiation of the radioisotope training program which was described in the previous annual report was postponed at the request of the Atomic Energy Commission until its division of Biology and Medicine could be established and become active. The program was, however, discussed with representatives of the University of Chicago in the fall of last year and was enthusiastically received by them. Following these discussions, Dr. J. R. Coe, Director of the Chemistry Division of the Laboratory, Dr. K. Z. Morgan, Director of the Health Physics Division, Dr. Alexander Hollaender, Director of the Biology Division and Dr. P. C. Aebersold, Chief of the Isotopes Branch, A. E. C. all offered the services of some of their staff members in a consultative capacity to the Institute. As a result a committee was formed under the chairmanship of Dr. George Boyd of the Chemistry Division and consisting of Dr. Overman, C. J. Borkowski, E. R. Tompkins, Henri Levy, Paul C. Tompkins and John A. Swartout. This committee rendered a great deal of assistance to the Institute in establishing the character of the training to be offered and making recommendations for the types of facilities needed for its conduct. Dr. Boyd, Dr. Overman, and Dr. Swartout worked up detailed plans for experiments to be conducted in the training program and the subject matter to be included in the lecture courses. Dr. P. C. Tompkins, Dr. Levy, and Dr. E. R. Tompkins developed plans and specifications for the radiochemical laboratories, counting room and lecture demonstration classroom and supervised the work of Mr. Mike Hawkins in preparing preliminary designs for hoods, chemical benches and other facilities of the Laboratory. This group maintained continuous day-by-day contact with the Engineering Design Section of the Atomic Energy Commission in Oak Ridge during the preparation of detailed engineering drawings for the necessary modifications to the Laboratory. The Engineering Design Section deserves high praise for the manner in which they assisted in solving the rather involved building problems.

The Institute was notified by the Division of Biology and Medicine of the Atomic Energy Commission in Washington early in February that this program had been approved by the Division and that it was most urgent that plans be completed for conducting the courses during the summer of 1948. At this time arrangements were made with the Oak Ridge National Laboratory to have Dr. Ralph T. Overman given a six-months leave of absence for the purpose of taking charge of this program. At the meeting of the Board of Directors on March 13, 1948, the Board appointed Dr. Overman as Acting Head of Special Training of the Institute, and Dr. Overman accepted this appointment on April 1, 1948. Detailed plans for equipping the laboratories and classrooms were completed at this time and a construction contract let to Roane Anderson Company for this work. At the same time all necessary equipment, supplies, and instruments were ordered and contact with individuals to serve as instructors in the courses was initiated.

It was decided to hold three four-week courses during the summer with the second course set aside for individuals from the universities cooperating with the Division of Biology and Medicine in its Fellowship program. Since the majority of the work consists of individual laboratory instruction, it was necessary to restrict enrollment to a maximum of 32 participants in each course. Application plans and a prospectus were sent out early in May and requests far in excess of the 96 vacancies have been received. The

Isotopes Branch of the Commission assisted the Institute in selecting the applicants. Preference is being given to those persons who are most nearly ready to begin research with radioisotopes. It is hoped that additional training sessions can be arranged during the fall and winter in order to more nearly meet the great demand for this type of training.

An excellent staff has been assembled to assist in the conduct of this training program. Instructors will be Dr. Ralph T. Overman, Acting Head of the Special Training Department of the Institute; Dr. H. M. Clark, Assistant Professor of Chemistry at Rennselaer Polytechnic Institute, Troy, New York; Dr. Henry Lanz, Jr., of the University of California, and Dr. C. L. Comar, Research Chemist at the University of Florida. All have had wide experience in radioisotope work. The Health Physics staff of the Oak Ridge National Laboratory, and the Isotopes and Biology Division of the Commission are furnishing personnel to assist in the conduct of the program.

Four rooms in the Institute Building have been set aside to conduct the radioisotope courses. A great deal of special equipment has been installed, and concrete shielding has been erected to protect personnel. One of these rooms has been set up as a counting room.

The three repeated courses will not attempt to cover any special field of application in chemistry or biology, but will be based on simple chemical experiments selected and designed to give participants a maximum knowledge and ability in the techniques of handling and carrying on research with radioisotopes. There has been a very serious need for training of this type since the Commission began the wide spread distribution of radioisotopes.

It appears that it will be desirable to conduct another series of radioisotope courses during the year, and plans are being made to continue this important activity.

Clinical Research Program

The Atomic Energy Commission called on the Institute in February to assume prime responsiblity for the initiation of a clinical research program in a specially prepared section of the Oak Ridge Hospital to study the recognition and treatment of malignant diseases with radioactive materials and radiations.

As an initial step in getting such a program underway, the Institute called a conference of representatives of 20 Southern Medical Schools to meet in Oak Ridge on March 1 and 2. In addition to the Medical School Representatives, Dr. Lucius A. Salisbury, Director of the Oak Ridge Hospital, Dr. Alexander Hollaender and Dr. Karl Z. Morgan, Directors respectively, of the Biology and Health Physics Divisions of Oak Ridge National Laboratory, and Dr. Paul Aebersold of the Isotopes Division of A. E. C. as well as Dr. A. H. Holland, Jr., Medical Advisor to the Commission at Oak Ridge, were invited and attended the meeting.

Dr. Wilburt C. Davison, Dean of the Medical School of Duke University, was elected Chairman of the meeting at the first session. He was asked by the Institute to make provision for a careful consideration, by a suitable committee, of the feasibility of the program. He was further requested to have the entire conference make recommendations to the Institute on the advisability and feasibility of undertaking this program, on an effective organization for its administration and direction, and to nominate individuals suitable for appointment to the Board of Medical Consultants to be named by the Institute.

Members of the Conference toured the Oak Ridge Hospital and the Biological Laboratories of the Oak Ridge National Laboratory during the afternoon of March 1, and Dean Davison reconvened the conference on March 2. After hearing a report of the special committee which met the evening before, the program was discussed in some detail by all representatives present. The conference then unanimously passed a resolution recommending that the Institute undertake the Medical Research program, and in the same resolution the group recommended that the Institute appoint a Board of Medical Consultants to exercise general supervision over the program. Chairman Davison then called on the conference to nominate individuals to be recommended to the Institute for appointment to the Board of Medical Consultants.

The Board of Directors of the Institute met on March 13 and after considering the recommendations of this Conference, unanimously adopted the following resolution:

"WHEREAS the United States Atomic Energy Commission has requested the Institute to arrange for, organize, and conduct a clinical research program for the study of radiation treatment of leukemia, cancer, and other malignant diseases in suitable facilities at the Oak Ridge Hospital, and,

"WHEREAS, at a conference of representatives of twenty Southern Medical Schools held on March 1 and 2, 1948, a resolution was adopted recommending that the Institute undertake such a program;

"NOW THEREFORE BE it resolved that,

"1. The Institute enter into negotiations with the United States Atomic Energy Commission for a supplement to its contract Number AT-40-1-GEN -33 to provide all arrangements necessary including provisions for reimbursement to the Institute for all costs which it incurs in the conduct of the program plus such an adjustment in the overhead allowance received by the Institute under this contract as may be required to adequately cover all additional overhead expense incurred by the Institute as a result of this program;

"2. The Institute hereby establishes an advisory board to be known as "The Board of Medical Consultants", which shall consist of not more than nine members and for which,

"a. The term of office of each member shall be three years except that for the first board, and depending on the size of the Board, two or three members shall be appointed for three year terms expiring June 30, 1951, two or three members for two year terms expiring June 30, 1950, and two or three members for one year terms expiring June 30, 1949;

"b. The relationship of each member to the Institute shall be that of a sub-contractor for consultant services with each corresponding sub-contract executed for the term of the appointment and making provision for payment to the consultant of a per diem consultant fee and traveling expenses in accordance with the reimbursement policy established in Article III, sec. 1 (c) of Contract No. AT-40-1-GEN-33 between the Institute and the Commission;

"c. The duties and powers of this Board shall be to make recommendations to the Institute with respect to the organizational structure for the clinical program; its research program, budget, and administrative policies; selection and salary of personnel involved in the program, including the Director, building, facilities, and equipment; and arrangements for participation by Southern Medical Schools;

"d. The meetings of this Board will be held on the call of the Executive Director of the Institute."

The following persons, all of whom were nominated by the Medical Conference of March 1 and 2, were named by the Board of Directors to the Institute's Board of Medical Consultants: Dr. Paul F. Hahn, of Meharry Medical College, Dean Wilburt C. Davison, Dean of the Duke University School of Medicine; Dr. George T. Harrell, of the Bowman Gray School of Medicine, Dr. Roy R. Kracke, Dean of the University of Alabama Medical School, and Dr. Vernon W. Lippard, Dean of the Medical School of Louisiana State University. These six members were asked to recommend the names of other persons to be appointed to membership on the Board of Consultants, with due attention being given to the additional talent necessary to bring the group to maximum efficiency.

Immediately following the constitution of the Board of Medical Consultants, steps were taken to draw up consulting contracts between the Institute and each member of the Medical Board, and each of these contracts has now been executed.

The Board of Medical Consultants met in Washington on May 6 with Dr. Pollard of the Institute, Drs. Shields Warren, J. Z. Bowers, and A. H. Holland, of the Commission in attendance, to work out the details of initiating the program. The following procedures were agreed upon at this meeting:

a. The normal channel of communication between the participating medical schools and the program will be through the Chairman of the regularly appointed "Cancer Committee" of a Medical School, or through any special committee appointed by the Dean of a participating university. Patients would be admitted to the program only by these committees.

b. The Board will select a person licensed to practice medicine and interested in clinical research and education to act as director of the program. With his aid there will be selected a small nucleus of responsible investigators (about 6 persons) in the general fields of

Hematology	Biochemistry	Pharmacology
Pathology	Radio Chemistry	Physiology
Internal Medicine	Health Physics	

plus a suitable group of technical and clinical assistants.

c. Business affairs will be administered through the Oak Ridge Institute.

To maintain continuity of research on available clinical material the Board will select a number of neoplastic diseases for special study. For each specific disease, a panel of consultants will be appointed from the staffs of the participating schools. Each panel, in cooperation with the permanent staff will

(1) Determine the specific details of the investigation
(2) Maintain a flow of patients to the Oak Ridge Hospital

d. Applications will be received by the Board from individuals who wish to investigate specific problems of their own, using materials available only at Oak Ridge. These individuals will be assigned as Special Project Directors for the duration of their project. They will be expected to furnish and maintain responsibility for their own patients.

Training Program

Details for establishing a training program also were discussed at the Washington meeting, and it was decided that facilities for the training of clinical resident physicians on both a long and short term basis should be set up, together with facilities for training physicians in practice and original investigators. These phases of the program will be established on the following bases:

a. About two long-term residents (one-two years) will be accepted to participate in the clinical investigative programs.

b. A number of residents will be accepted for three-month periods of training in the use of radioactive materials and the handling of patients being treated with these materials.

c. Physicians in Practice or teaching may be accepted for varying periods of time, both for training in the use of radioactive materials and to participate in the investigative program. This program will be coordinated with the instructional facilities already organized by the Oak Ridge Institute.

d. National Research Council Fellows will be accepted to conduct original research under the supervision of the permanent staff and consultants.

e. Non-clinical medical investigation may be accepted but will, in general, be referred to the more general program of the Institute.

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The Board also authorized the Director of the Clinical Research Program to set up an information activity to coordinate the program, and to keep participating schools and individuals aware of the activities and opportunities available.

Dr. Marshall Brucer was elected Chairman of the Board of Medical Consultants.

The Board of Medical Consultants held a second meeting in Washington on June 15, with Dr. Pollard in attendance, and took preliminary action toward the selection of a suitable Director of Clinical Research.

Participating Programs With Member Universities

The Institute served as co-sponsor of a Conference on the Use of Radioactive Isotopes in Agricultural Research held at the Alabama Polytechnic Institute from December 18 to 20, 1947. More than 400 agricultural research workers, chemists, and others from throughout the South attended the conference.

This conference is an excellent demonstration of how the Institute can serve its member universities in special projects. For this conference, the Institute arranged with the Commission to secure the necessary radioisotopes, assisted in obtaining the participating personnel, and shared a part of the cost of the conference. The program of the conference was as follows:

December 18

FUNDAMENTAL CONSIDERATIONS

Morning Session
W. G. Pollard, Presiding

TECHNIQUES OF TAGGED ATOM RESEARCH
S. F. Carson, Oak Ridge

RADIOACTIVITY AND RADIO-ISOTOPES
Fred Allison, Auburn

Afternoon Session
Eric Rodgers, Presiding

ISOTOPES AVAILABLE FOR RESEARCH
Paul C. Aebersold, Oak Ridge

THE MEASUREMENTS OF RADIATION BY VARIOUS METHODS
Paul W. McDaniel, Washington

PROTECTIVE PRECAUTIONS IN THE HANDLING OF RADIOACTIVE MATERIALS
G. William Morgan, Oak Ridge

Night Meeting
Russell S. Poor, Presiding

CONTRIBUTIONS OF THE ATOMIC ENERGY COMMISSION TO AGRICULTURAL RESEARCH
John Z. Bowers
Assistant to the Director,
Division of Biology and Medicine
United States Atomic Energy Commission

December 19

PLANT PHYSIOLOGY, SOILS, AND HORTICULTURE

Morning Session
Nathan H. Woodruff, Presiding

AGRICULTURAL RESEARCH WITH RADIO-PHOSPHOROUS
S. B. Hendricks, Beltsville

STUDIES OF CHLOROSIS USING RADIOACTIVE PHOSPHOROUS AND IRON
Orlin Biddulph, Pullman

AGRICULTURAL RESEARCH WITH RADIOACTIVE SULFUR AND ARSENIC
M. D. Thomas, Salt Lake City

Afternoon Session
Paul W. McDaniel, Presiding

DEMONSTRATION OF A TYPICAL TRACER EXPERIMENT
Ralph T. Overman, Oak Ridge

Inspection Tour of Laboratories

Night Session
M. J. Funchess, Presiding

INDUCED AND NATURALLY OCCURRING MUTATIONS IN RELATION TO HETEROSIS AND THEIR VALUE IN PLANT AND ANIMAL IMPROVEMENT
Donald F. Jones, New Haven

December 20

NUTRITION AND ANIMAL HUSBANDRY

Morning Session
W. A. Lazier, Presiding

SOME BIOLOGICAL AND MEDICAL USES OF RADIOACTIVE ISOTOPES
G. Harold Copp, Berkeley

TRACER STUDIES WITH C14 URETHAN
Howard B. Skipper, Birmingham

NUTRITION STUDIES WITH RADIO-COBALT AND RADIO-COPPER (Motion Pictures)
George K. Davis, Gainesville, Florida

The Institute is anxious to cooperate with other member universities in conducting similar activities in the field of nuclear energy.

The Institute served as co-host to the 1948 meeting of the Southeastern Section of the American Physical Society held in Oak Ridge on April 9 and 10. President Graham delivered one of the principal addresses at this meeting, and Dr. Pollard served as a member of the Program Committee which organized the meeting. The Institute conducted a tour of the Oak Ridge Area for those attending the meeting, supplying busses and commentators for the 400 physicists in attendance. The Institute has offered its services as host and sponsor for the meeting of the Southeastern Section in April of next year, although this offer has not yet been acted on by the Society.

Award for Papers

The Board of Directors has devoted considerable time to the matter of sponsoring activities other than the regular Institute programs that will stimulate the development of scientific research and training in member universities. The first such step was formally approved at the March 19 meeting at which the Board decided to make three annual awards of $500 each for papers of distinguished merit in the fields within the province of the Institute. These awards are open only to staff members or students from the member universities and will be paid from the Institute's own funds. Eligibility conditions, rules, and other information on the awards will be published prior to the beginning of the 1948-49 school year.

It is expected that similar programs will be developed as the Institute reaches maturity.

Supplementary Graduate Training Program

This program, which is conducted purely as a service function to Oak Ridge, continues to be an important factor in enabling the Commission and its contractors to retain highly skilled personnel. Because the Institute does not grant academic credits in its own name and because the supplementary program is quite distinct from the regional and national programs of the Institute, this program has been sub-contracted to the University of Tennessee.

Under the terms of the contract, the Institute supplies the building facilities and the necessary equipment and supplies for conducting the program, and the University supplies all the necessary personnel. The Institute has supplied five classrooms for the program, two well equipped chemistry laboratories, a biology laboratory, a physics laboratory, and an instrument shop. The chemistry laboratories contain standard benches with outlets for compressed air, vacuum, gas, hot and cold running water, glass blowing tables, and other equipment found in a well supplied chemical laboratory.

The physics laboratory is equipped with AC and DC voltage and all necessary equipment to conduct laboratory work in atomic physics. The biology laboratory similarly is well equipped with storage cabinets, two incubators, a refrigerator, an oven and autoclave, together with microscopes and other biological equipment.

Courses for the masters and doctors degrees in Chemistry, Mathematics, and Physics are offered through the University of Tennessee Graduate School Branch at Oak Ridge, and some of the University's best teaching talent has been assisgned to Oak Ridge.

Attendance at the Oak Ridge Branch during the fiscal year was as follows:

Summer Session, 1947	56
Fall Quarter, 1947	202
Winter Quarter, 1948	132
Spring Quarter, 1948	108

Forty-eight employees are now working on their doctoral degree through this program. A total of 235 different students participated in the program during the school year.

Originally, classes were held only at nights and on week ends, but an arrangement has been worked out whereby some students also attend classes on Tuesdays and Saturdays, with the attendant's pay being reduced by 20 per cent to compensate for his absence from work one day each week.

The University is conducting this program at considerable cost to itself. It is expending about $73,200 annually out of its own funds over and above the amount reimbursable by the Commission.

The Institute refers all requests for information on this program to the University of Tennessee and takes no part in it except for supplying the facilities and serving as a liaison agent between the University and the various contractors on questions of leaves of absences, schedules, and similar matters.

The building needs of the University for the conduct of this program was a major factor in enabling the Institute to receive greatly expanded quarters. The fact that it received such quarters has been invaluable in organizing the radioisotope training program, the medical research program and similar activities. The Institute has since been forced to obtain additional building space to house its activities.

SECTION III. ADMINISTRATION AND ORGANIZATION

Election of Executive Director

The Nominating Committee selected to recommend nominations to the Board of Directors for the position of Executive Director reported at the Board Meeting of October 31, 1947. The Committee recommended that Dr. Pollard be named as Executive Director, and with the nominee absenting himself, the Board unanimously elected Dr. Pollard to the post.

On informing Dr. Pollard of his election, Dr. Seitz advised him that it was the desire of the Board that he give primary consideration to arrangements which would permit him to maintain his scientific interests, engage in scientific research, attend scientific meetings, and serve as a consultant to research groups in Oak Ridge where appropriate. It was emphasized that the position should not be purely administrative in character, but on the contrary should be made to serve as a medium for expressing the scientific leadership of the Institute.

Organization

As the Institute program broadened, it became evident that a greatly expanded organization was essential for it to function properly. At the March 13 meeting, the Board of Directors authorized the Executive Director to assemble a considerably expanded administrative staff to perform the increasing work of the Institute. The Board in effect directed a major reorganization of the Institute staff along lines shown in detail below.

An office of business management was established to perform the standard budgetary, fiscal, accounting, and other routine management affairs of an organization similar to the Institute in size and character. The Board also authorized the appointment of Mr. J. W. Mumford, a man of wide experience in business matters, to the position of Business Manager. As such he will direct the office of Business Management and assemble the necessary personnel, with the approval of the Executive Director, to perform the duties of this office.

A University Relations Division was authorized to assume responsibility for one of the major functions of the Institute. This Division will supervise and administer the Graduate Training Program, will be charged with the placement of university scientific staff members in Oak Ridge laboratories, will administer the Supplementary Graduate Training program sub-contracted to the University of Tennessee, and assume responsibility for all activities of the Institute involving direct services to, or relations with, universities and other research institutions outside of Oak Ridge, and with university faculty and graduate students. The University Relations Division will have the assistance of all other departments where necessary to carry out its activities.

A Special Training Division was set up to conduct programs of training in special techniques of research developed on the Atomic Energy project. The first such program is the series of radioisotope courses to be held at Oak Ridge this summer. This Division will be charged with responsibility for the preparation of detailed plans for each training course, for the conduct of correspondence in connection with such training programs, for the preparation of announcements and other notices, the development of procedures for application and admission to such programs, and similar activities. During intervals between training programs, the Head of this Division and his assistant will engage directly in research and training at the Oak Ridge National Laboratory in connection with the Institute's Fellowship program at the Laboratory.

At the March 13 meeting, the Board of Directors approved the appointment of Dr. Ralph T. Overman as Acting Head of the Special Training Division. Dr. Overman is a Senior Research Chemist at Oak Ridge National Laboratory and has played a leading role in research leading up to the wide-scale production of radioisotopes for use in research. He was granted leave of absence by the Laboratory to join the Institute staff.

A Medical Division was authorized to conduct the Medical research program assigned to the Institute in March. The direction of the work of this department, the formulation of its administrative structure and technical supervision, and the development of the Research Program is the responsibility of the Board of Medical Consultants. The Board will advise the Executive Director of the Institute concerning a suitable structure for the resident staff of the research hospital, and will assist in the appointment of suitable individuals to positions in the programs.

In addition to the conduct of the Medical Research Program, this Division will cooperate with the Academic Division in the maintenance of adequate relations with Southern Medical Schools.

Legal Counsel

The Board of Directors early recognized the necessity of employing legal counsel to assist and advise the Executive Director in the negotiations of contracts, in complying with various Federal and State laws in the operation of the Institute, and in many other fields. At its third meeting, on June 30, 1947, the Board of Directors authorized the Acting Executive Director to engage Mr. Charles D. Snepp, of the firm of Anderson and Snepp, of Knoxville, as counsel for the Institute. Mr. Snepp has been of invaluable assistance to the Institute during the past year.

Assignment of Building

The Institute headquarters was moved in October from an office in the Administration Building to greatly expanded quarters in Building 2714-G. This building, which was originally intended as a research laboratory for the Manhattan District, contains almost 20,000 feet of floor space and is well constructed of yellow tile. Although inadequate to house the expanding activities of the Institute, the building is the best available at this time. It contains eight offices, twelve classrooms and laboratories, a workshop, limited storage space and related facilities. Two of the laboratories have been re-designed for use in the radioisotope training course during the summer, and concrete shielding has been erected where necessary. A counting room has been set up, and other laboratories have been fully equipped for use in biology, chemistry, and physics.

Lack of library and office space is the most serious deficiency in the present building. The library has space for no more than 10 students and readers, and more than 200 persons are attending various Institute Programs. Although office space is at a premium in Oak Ridge, the Institute received 2,000 feet of additional office space in the City Administration Building early in June, and the business and executive offices of the Institute were moved there on June 9.

The Institute has submitted, at the request of the Commission, estimates for its building needs over the next five years. It is expected that these needs will be met by construction of new, permanent-type buildings, with architecture in keeping with the academic background of the Institute. The following requirements were submitted as the minimum needed by the Institute for the next five years, as nearly as such requirements could be determined by present knowledge:

Central Administrative Office Space	12,000 square feet
Conference Space	400 square feet
Auditorium (to seat 500 people)	5,200 square feet
(plus 2 large lecture rooms to open into auditorium when needed)	1,200 square feet
Library	3,400 square feet
Recreation room	2,000 square feet
Vault	400 square feet
Special Training Division (Radioisotope laboratories, counting room, animal room, store rooms, classrooms, and research laboratories)	7,250 square feet
University Relations Division (Laboratories, classrooms, storerooms, preparation rooms, and greenhouse, for physics, chemistry, biology, and agriculture)	7,470 square feet
General Classrooms (four)	1,500 square feet
Shop	800 square feet
Warehouse and storage space	17,900 square feet
Total (approximate)	60,000 square feet

Personnel Policies — The Institute, in so far as its contractual obligations permit, is establishing a university type rather than an industrial type atmosphere in its administrative headquarters. The contract with the Commission authorizes very liberal personnel policies to be established. Major provisions of employment policies are as follows: a fourty-hour work week, six holidays annually, up to 10 days excused absences with pay under exceptional circumstances, two weeks vacation after one year of service, and one week during the first calendar year if employment began prior to July 1, sick leave of [illegible] days annually for the first year with increments in succeeding years up to 55 days for the fifth year and thereafter, and a retirement plan through the Teachers Annuity and Insurance Association under which contributions are made as follows:

	By employee	By employer
On first $250.00 of basic monthly salary	2½%	7½%
On that portion in excess of $250 monthly	5%	5%

The Institute also will carry life and health insurance on each employee as soon as the required number of persons have been employed.

Initiation of these employment policies has resulted in the establishment of very high worker morale on the part of the Institute employees.

ADMINISTRATIVE PERSONNEL NOW EMPLOYED BY INSTITUTE

Beck, Harold D., Jr.	McClannahan, Barbara O.
Brown, Dorothy A.	Mumford, J. W.
Burton, Betsy A.	Odom, Lois E.
Couey, James H.	Overman, Ralph T.
Dinsmore, Donna M.	Pollard, William G.
Disney, William G.	Rose, J. W.
Donnell, Mary C.	Russell, Mary E.
Frost, Arthur H., Jr.	Sharp, Dorothy M.
Hill, Hugh Paul	Vaughn, Charles L.
Hull, Abbie R.	Whited, Betty P.
Johnson, Dixon	Wood, Mary J.
Livesey, Robert L.	

INSTRUCTORS FOR RADIOISOTOPE PROGRAM

Clark, H. M.	Finkle, Ray D.
Comar, C. L.	Lanz, Henry

Contract With Commission — Negotiations on the Institute's definitive contract with the Commission continued through a good part of the year, and the contract itself finally signed on May 24, 1948. It replaces the temporary letter contract under which the Institute has operated since March, 1947, and will remain in effect until December 31, 1951. In general, the provisions of the contract

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are the same as those contained in the earlier letter contract except for their more permanent nature. Provisions are made in the contract for carrying on the Graduate Training Program, Research Participation Program, the Supplementary Graduate Training Program, the Radioisotope Training Program and other special programs in the field of nuclear and related sciences. A supplement to the contract makes provision for the Clinical Research Program of the Medical Division.

The contract also calls on the Institute to serve in an advisory and consultative capacity to the Commission. It establishes the necessary contractual relationships under which the Institute is reimbursed for the cost of the work it carries on, with the exception of the salary of the Executive Director and the expenses of meetings of the Board of Directors. The contract makes provision for a fixed overhead allowance, readjusted annually and payable in equal monthly instalments to cover miscellaneous expenditures for which provision for direct reimbursement has not been made. Appendix A of the contract defines employment policies, leaves of absence, benefits, annuities, insurance and similar matters with respect to the Institute employees.

APPENDIX I

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CARBIDE AND CARBON CHEMICALS CORPORATION
UNIT OF UNION CARBIDE AND CARBON CORPORATION

POST OFFICE BOX P
OAK RIDGE, TENNESSEE

January 9, 1948

Board of Directors
Oak Ridge Institute of Nuclear Studies
P. O. Box 117
Oak Ridge, Tennessee

Attention: Professor Wm. G. Pollard
Executive Director

Gentlemen:

Following our conference Wednesday afternoon, plus the several subsequent conversations between smaller groups, it may be helpful for us to try to indicate, a bit more in detail, just what the Carbide and Carbon Chemicals Corporation group believes can (and should) prove sound bases for cooperative efforts with the ORINS and Southeastern Universities groups. These bases do not represent all the possible items and these here listed have not been thought through in detail. They do represent a good start.

1. First of all we believe the proposals of the AEC are "firm" and that---within the scope of the contractual obligations as finally agreed to---the Chemicals Corporation can operate the X-10 facilities as a true "National Laboratories" carrying out the basic research, engineering developments and small-scale production--as desired by the Commission. The two beliefs are fundamental: Without them the Chemicals Corporation would not be interested in proposals of the AEC.

2. We would like the University groups to feel an interest in, and obligations for, the successful prosecution of the basic research part of the programs previously included in the X-10 set-up. In line with this wish, we would like the University groups to assist in planning the personnel and scientific program required for the basic work.

It would be desirable if the University groups---through a Scientific Advisory Committee (Steering Committee, or named as you wish)---appointed by you---would outline, or suggest the outline for the basic program and advise regarding the technical and organizational programs. Current initial operations will, perforce, have to consist of extensions of current programs recommended by personnel from the Monsanto-University Chicago X-10 organization, but we will welcome comments, criticisms or approval.

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Later, when a satisfactory new organization is established, we expect the personnel to submit annual programs---on which we will appreciate your review, criticisms and approval. Insofar as your suggestions fall within our contractual obligations with the Commission, we will attempt to cooperate with you.

We would prefer that the Coordinator we appoint for the basic research program be a man recommended, or approved, by your group. Preferably, he should be furnished by your group. We will welcome assistance.

Help along other personnel lines will be welcomed by the Chemicals Corporation from the University group. These include (potentially) professors on Sabbatical leave, or on an exchange basis; as well as graduate students, within (or in addition to) the ORINS group. Details regarding the last-named should be worked out. Graduate and postgraduate students leaving your universities are urged to consider permanent employment with Chemicals.

3. The Chemicals Corporation proposes to follow a very liberal policy regarding publications from the staff of the Clinton National Laboratories. Only two criteria are planned: (1) Technical quality to reflect credit on the individual and the group, and (2) Security regulations. A subgroup from the Universities might well be chosen to pass on (1) and to make suggestions on (2). The Chemicals Corporation will put no obstacle in the way of publications indicating the connections of the authors with their universities or the ORINS, nor does the Chemicals Corporation plan to insist on designation of the corporation's connection.

4. In an effort to maintain even closer relationship with the University viewpoint than is now foreseen from ORINS contacts, the Chemicals Corporation plans to seek individual personal consulting contracts with various academic scientists. It is hoped that these contracts (at least the majority of them) can be placed with scientists from the Southeastern Universities group. We would appreciate suggestions or nominations and advice from your group.

5. One final, though not insignificant, item should be here listed. We feel that the Clinton Laboratories, to be a true National Laboratory, will require facilities additional to those now at X-10. Specifically, but only as an example, we believe that a large cyclotron is desirable, and easily possible at Y-12, and really necessary if the Southeastern Universities are to make the progress we hope for and expect. We have asked the Commission for such a cyclotron and have every reason to believe it will become available---and quickly! We hope you can consider this intention in making your plans for basic work and will cooperate fully in securing optimum yields from these facilities. Here again we will welcome your assistance.

6. Most of your groups understand the geography and physical set-up at Oak Ridge. It is hoped that a single large operating group (the C&CCC) can (with the help of local Commission personnel) develop improved living and working conditions within the area. This applies particularly to housing---a point of importance in considering exchange personnel or individuals for short stays in Oak Ridge.

At least passing reference should be made to our belief that there is room for improvement (nationwide) in the relationship between American industry and Universities. The set-up at Oak Ridge, where so many new and unusual facilities are available, would seem to afford an excellent opportunity for cooperation to the mutual advantage of Universities and many industrial organizations to whom (otherwise) such facilities would be inaccessible. We believe there is a fruitful field here.

At the risk of appearing repetitive, we believe the above are at least preliminary bases for starting work or contacts with your University groups. Furthermore, we believe they justify an optimistic approach to the many problems we know will arise. A four-year contract offers a good "line of departure". Progress will depend on many factors---not the least of which will be your help in maintaining a truly "National Laboratory"--or even a "Sectional Laboratory". What further bases can your group suggest to the further advantage of the Universities and the Atomic Energy Commission?

Very sincerely yours,

CARBIDE AND CARBON CHEMICALS CORPORATION

/s/ George T. Felbeck
Vice-President

GTF:bd

C O P Y

APPENDIX II

C O P Y

UNITED STATES
ATOMIC ENERGY COMMISSION
Washington 25, D. C.

April 7, 1948

Dear Dr. Graham:

During the past few months there have been some inquiries by universities concerning the best way in which they can cooperate with the Atomic Energy Commission in developing the National Laboratory at Oak Ridge. As President of an association of universities developed for this purpose, namely the Oak Ridge Institute of Nuclear Studies, you can most appropriately advise the universities in this matter.

Out of my experience with the TVA over a period of years in the development of a close working relationship with the Universities of the region, I know how important and helpful such cooperation between a public technical enterprise and the Universities can be. While the Nation's atomic energy program is markedly different from the TVA program in many respects, still in the matter of close working relations with Universities there is helpful precedent.

As to how best this essential cooperation can be made effective, this is a question that will require time and experience to answer. The Commission is strongly committed to the idea embodied in the Oak Ridge Institute of Nuclear Studies as probably the most effective means yet devised to achieve this cooperation. It is, furthermore, a means that will lend itself to adaptation from time to time in accordance with the requirements of the paramount responsibilities of this Commission to the country. A region-wide agency, i.e. the Oak Ridge Institute, joining the universities into a specialized instrumentality seems well adapted to the needs of the situation, both from the viewpoint of the necessities of the Nation's whole atomic energy development and of the South and its institutions.

There has been considerable misapprehension generally about the recent realignment of the reactor phase--the most important phase--of the development program. The Commission was forced by experience to conclude that success in the urgent work of developing nuclear reactors could be best attained by placing this work largely under one direction; and that the best prospects for this--everything considered--would be at the Argonne National Laboratory. This decision was in no sense whatever a reflection of any kind on the management of the Oak Ridge National Laboratory or its notable working force. The other basic research activities at Oak Ridge must now be strengthened, in order to advance the Nation's interests most rapidly.

C O P Y

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It is in the types of basic research intensified at Oak Ridge, not reactor development, that the Universities of the South have the greatest interest--so it would seem to me--and have the greatest opportunity to contribute to this Nation's atomic energy program. The Commission, its Oak Ridge Manager, Mr. John Franklin, and the Carbide and Carbon Chemical Company, the contract operator at Oak Ridge, are prepared and eager to have the full participation of the Universities of the region--through their creation, the Oak Ridge Institute of Nuclear Studies--so that all of us may carry forward basic research in a way and on a scale such as the South has never seen before.

A new era of scientific research and training is opening for the South; this is my confident belief. The fact that an industrial concern of long experience is combining with a Government Agency, The Atomic Energy Commission, and with a union of Universities, presents a great challenge. For just this combination has never been tried before, and in terms of the interest of the South and its technical advance, seems to hold out much that is hopeful, and potentially of great value. For the South needs expanded academic training opportunities for scientists and it also needs industrial development experience and know-how. These, together with some of the finest and most costly laboratory facilities in the world, can produce great results for the training of the South's young People, for the good of the country, and, we may hope for the ultimate benefit of mankind.

So I say, the best way in which the universities can cooperate is in helping the Commission, its Manager, Mr. Franklin, the Carbide Corporation and the to-be-named Director of Oak Ridge National Laboratory, to make this research institute a success. It is the Commission's stated intention that the Oak Ridge Institute will work closely with the Director of the Oak Ridge Laboratory and with the Commission in charting the course of this research work, in assessing the program, in working out improvements that will further the Commission's work and the work of the Universities. This process of consultation between the people who man the Laboratory itself, the Universities, the operating corporation, and the Commission, surely provides a means for achieving the maximum usefulness of these great facilities and making the most of thisgreat opportunity.

I am no perfectionist: I recognize that in human affairs (and even pure science is carried on by human beings) it is not possible completely to satisfy the views of everyone. I do not expect this to happen here. But given the right spirit I do believe the results of this effort will be generally satisfactory to most of the varied interests and responsibilities involved.

Sincerely yours,

/s/ David E. Lilienthal

David E. Lilienthal
Chairman

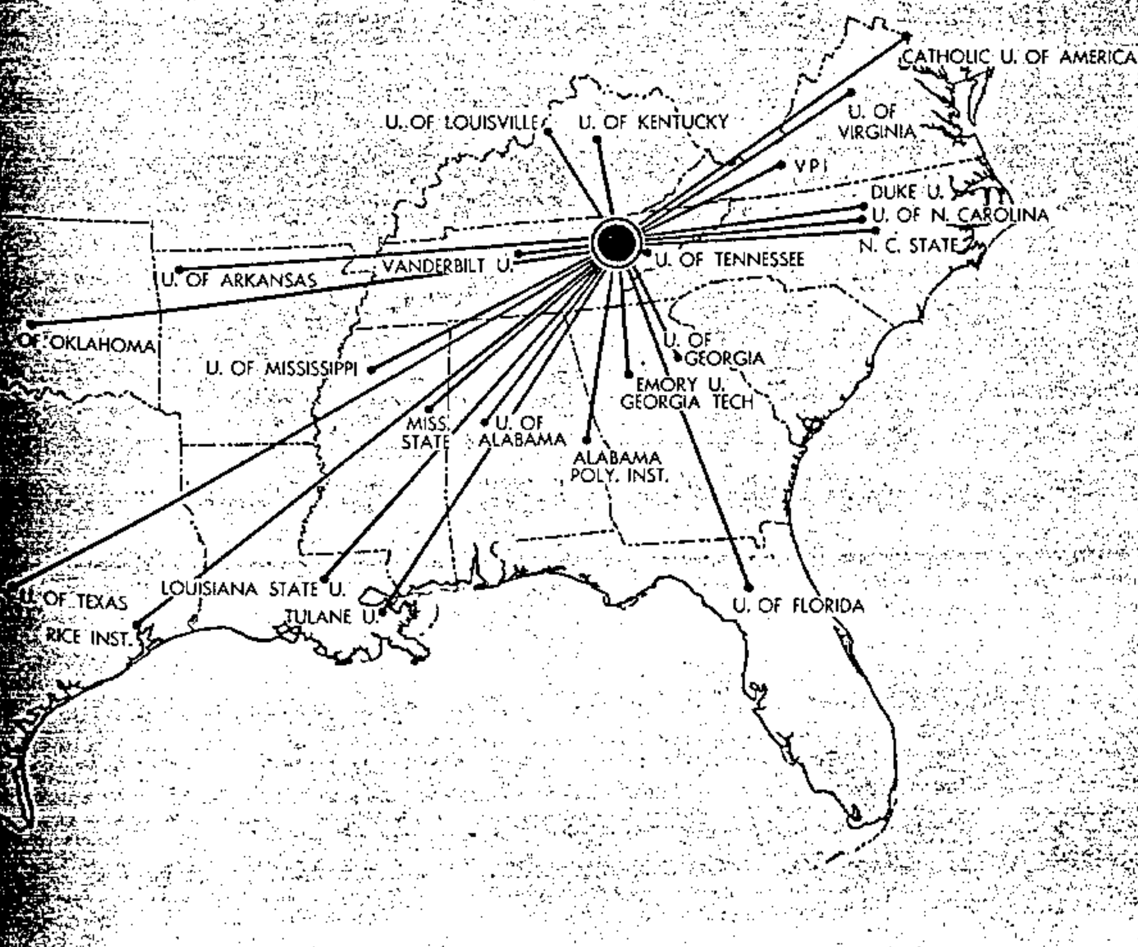
Dr. Frank P. Graham
President
University of North Carolina
Chapel Hill, North Carolina

DEL:mjb

1948-49

OAK RIDGE INSTITUTE OF NUCLEAR STUDIES

Annual Report 1948-49



OAK RIDGE, TENNESSEE

MEDICAL DIVISION

Marshall Brucer, M. D., Chairman

By the beginning of the current fiscal year, the Board of Medical Consultants of the Institute had pretty well sketched out the outlines of the medical program. This group of men, representative of the best the South had to offer and of a calibre to command respect everywhere, spent many an hour laying out the program. They journeyed to Oak Ridge, to Washington, to North Carolina, and a half dozen other places for conferences and meetings. Finally, on September 30, the Board approved the Basic Medical Plan, a condensed copy of which is attached at the end of this report.

With the plan outlined, the Board of Medical Consultants then began a searching review of the whole plan to make sure that it was feasible and to offer sound hope of good to come from the money to be spent. At the November meetings, then, the Board took a critical look at its handiwork. A synopsis of the Board's review follows:

It had been suggested that government money might better be spent at the Southern universities where there are already groups of highly trained investigators in the medical sciences and where patients are more readily available. It had also been suggested that the program would be crippled by the restriction of the study to cancer. Objections had been raised concerning the inaccessibility of Oak Ridge, its lack of clinical facilities, and the security regulations implied in a program located at an Atomic Energy Commission installation. It had also been pointed out that radioisotopes have not shown evidence of fulfilling the therapeutic expectations originally predicted for them. It had been pointed out to some members of the Board that facilities already exist for medical research in both the field of cancer and in the field of radioisotopes at well-established centers throughout the country.

The Board decided that there are disadvantages to medical research at Oak Ridge, but the Board also considered certain accompanying advantages. Although Oak Ridge does not already have a staff of medical scientists it does have a group of scientists trained in physics, chemistry, and biology which would be difficult to match at any single university and would open up whole new approaches to the study of cancer. The Board felt that all investigations are set up within restrictions and that the limitation to a study of a field as broad as cancer is almost no restriction at all. Although it is true that patients would be more readily available at any university medical center it is highly probable that such a placement would result in a domination by that center. It was considered one of the purposes of the program to make Oak Ridge more available to all of the Southern medical schools, and to discourage its domination by any small group of individuals. Moreover, the lack of clinical research facilities at Oak Ridge can be relieved only by constructing such facilities; and a program such as it proposes is the logical agency to supplement the existing facilities at Oak Ridge. The Board was not so much impressed by current disappointments in the use of radioisotopes as by the possibility of use in as yet uninvestigated fields. The Board of Medical Consultants was also of the opinion that the proposed program will be more likely to succeed as a major activity at a center devoted to the study of radioactivity than it would at any single university medical center where it would be only one of many important clinical research efforts. In the light of such discussion, the Board passed the following resolution:

> "RESOLVED, that the Board of Medical Consultants of the Oak Ridge Institute of Nuclear Studies, assembled at New Orleans, Louisiana on 17 November 1948, after much discussion and mature deliberation concerning both the advantages and disadvantages of establishing a medical program at Oak Ridge, and being cognizant of the objections which have been raised against such a program wish to reaffirm the March 2, 1948 resolution of the representatives of the Southern medical schools that the Oak Ridge Institute of Nuclear Studies undertake the proposed Medical Program at Oak Ridge."

A concurrent problem to that of establishing a basic philosophy and program was the matter of picking a competent man to lead the Medical Division. The demand for medical personnel in research had never been greater. During its deliberations the Board screened more than 90 prospects. *At its meeting* on November 17, the Board recommended that Dr. Marshall Brucer, then of the Department of Physiology, University of Texas, be named Chairman of the Division.

Dr. Brucer reported to Oak Ridge on December 30 and since that time has pursued his work with vigor and skill. He has recruited the nucleus of an outstanding staff, the medical building was under construction at year's end, bids for laboratory equipment were out, hoods for the use of radioactive materials had been designed, and the entire program was progressing in a most satisfactory manner.

ADDITIONAL STAFF

The Board then aimed at obtaining a strong staff in depth. Since the Division is approaching the problem of the medical use of radioisotopes as primarily a pharmacological one, the Division has been unusually fortunate in adding Dr. H. D. Bruner as Principal Scientist and the number two man in the Division. Dr. Bruner, an outstanding research scientist was Professor of Pharmacology and head of the Department at the University of North Carolina Medical School. Dr. Bruner received his bachelors, master's and medical degrees at the University of Louisville and did his Ph. D. work under Dr. A. J. Carlson at the University of Chicago. He did wartime research on OSRD projects at the University of Pennsylvania Medical School and at this time has more than 25 research papers to his credit.

There was need of a research man also trained as an internist, particularly in the period before the residence program is set up. This situation has been well taken care of in the addition of Dr. Gould Andrews to the staff as Senior Scientist. A specialist in hematology, Dr. Andrews is well-equipped to serve as an internist. Prior to joining the Institute staff, Dr. Andrews was director of cancer training at the Stritch Medical School of Loyola University in Chicago. He received his training at the University of Michigan Medical School.

DR. HARRY BRUNER

DR. MARSHALL BRUCER

DR. GOULD ANDREWS

DR. JESSE PERKINSON

DR. JACOB FURTH APPOINTED PATHOLOGIST

An excellent example of the unusual situation that makes Oak Ridge a splendid research center is seen in the appointment of Dr. Jacob Furth, internationally-known pathologist, as Pathologist to the Medical Division, even though Dr. Furth is actually on the staff of the Biology Division of the Oak Ridge National Laboratory as Head of the Pathology and Physiology Section. This unusual arrangement holds great promise for effective research. Dr. Furth brought with him to Oak Ridge a large number of extremely valuable laboratory animals from his former post at Southwestern Medical College. He is the author of more than 100 research papers and is Vice President of the American Association for Cancer Research and a member of the Editoral Board of the Journal of the National Cancer Institute and the magazine Cancer Research. He is a recipient of the Gold Medal of the American Medical Association for his work on leukemia, and again, he was elected for honorable mention by the Association for his work on ovarian tumors.

Both Dr. Bruner and Dr. Andrews joined the staff on July 1. Slated to come to the Division on August 1 is Dr. Jesse Perkinson, Assistant Professor of Biochemistry at the University of Georgia, who is joining the staff as Senior Scientist in Biochemistry.

With these four as the nucleus, the Board has laid the foundation for an outstanding staff.

A number of technicians already have been employed to assist in the work of the Division, together with necessary office personnel.

ARCHITECTURAL LABORATORY DESIGN AND CONSULTANT SERVICE

With the rapid increase in the use of radioactive materials and the need for special facilities, the Institute receives numerous requests for advice on laboratory design and building construction for both safety and efficiency. The Medical Division has supplied this type service to the following organizations and individuals to date:

The University of Tennessee Medical College architects in Memphis, through Dr. Douglas Sprunt, who is in charge of the construction of the cancer research facilities in Memphis.

The Medical College of Alabama at Birmingham, through Dr. John Bruhn, Chairman of the College construction committee.

The University of Virginia Medical School at Charlottesville.

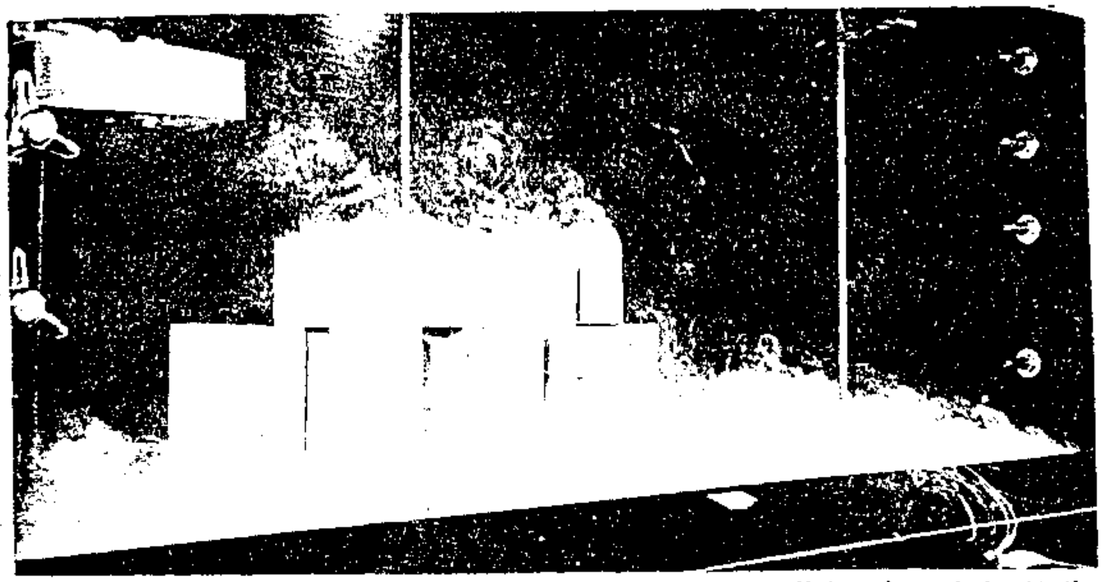
The University of Texas Cancer Research Unit at Houston.

Dr. L. H. Gray of the Radiotherapeutic Research Unit of Hammersmith Hospital, London, England.

RADIOCHEMICAL LABORATORY DESIGN

Probably the most important single piece of equipment in the radiochemical laboratory is the fume hood. Since the hoods currently available were either unsatisfactory or too expensive, steps were taken early to design a suitable hood. A number of conferences were held with various specialists in health physics, radiochemistry, radio-physics, and engineering in the Oak Ridge area concerning the requirements for laboratory design within the scope of the hospital usage of radioisotopes. Later, talks were held with representatives of various laboratory and equipment manufacturers. A preliminary drawing and statement of specifications for an adequate radioactivity fume hood was drawn up and submitted to four of the major laboratory furniture manufactures. Representatives from the Oak Ridge National Laboratory, the Isotopes Division, and the Institute were called to the experimental laboratory of the E. H. Sheldon Company, laboratory equipment manufacturers in Muskegon, Michigan. Following this conference, an experimental hood was constructed by the Sheldon Company and set up in the Training Building of the Institute. This hood was given exhaustive tests in April, and on April 21st, representatives of interested organizations in Oak Ridge and various laboratory furniture manufacturers were invited to inspect this completely new design in hood construction. The hood has been approved by both the Medical and Special Training Divisions of the Institute.

The redesigning of the radioactivity fume hood is one phase of a current program designed to standardize, within certain limits, many of the items of equipment which are necessary in the handling of radioactive substances. A series of conferences are under way with the U. S. Plywood Corporation concerning the use of bonded stainless steel and plywood; with the Oak Ridge National Laboratory concerning the design of remote handling equipment; with the Isotopes Division and other handlers of isotopes concerning the adoption of a standard radioactivity hazard symbol; with the Corning Glass Works and the T. C. Wheaton Company concerning the adoption of standard laboratory radioactivity glassware; and with a number of venders of metallurgical products concerning design questions on shielding blocks.



RADIOACTIVE FUME HOOD designed and constructed by collaboration of the Medical Division, Special Training Division and the E. H. Sheldon Company of Muskegon, Michigan. The major change in the hood is the reduced air flow.

CONSULTANTS

It was recognized early that the permanent Oak Ridge staff would be a nucleus only. For the Division to function as conceived, active participation by the cooperating medical schools was deemed essential. Additionally, medical scientists from outside the region with unusual talents would be a valuable asset to the Division. Consequently, the Board has devoted considerable time to the matter of assembling an outstanding consulting staff. At present this staff consists of thirteen individuals and is being expanded rapidly. The present consultants to the Division are as follows:

Lester Van Middlesworth, Ph. D.
Instructor, Department of Physiology
University of Tennessee

John L. Wood, Ph. D.
Associate Professor of Chemistry
University of Tennessee

Charles Allen
Associate Professor of Anesthesiology
University of Texas Medical Branch

John M. Bruhn, Professor and Chairman
Department of Physiology and Pharmacology
University of Alabama

G. W. Baldridge
University of Pennsylvania

Cornelius T. Kaylor
Associate Professor of Anatomy
University of North Carolina

Jerome S. Harris
Associate Professor of Pediatrics and Biochemist
Duke University

Philip Handler
Associate Professor Biochemistry and Nutrition
Duke University

Arthur C. Guyton, M. D.
Associate Professor of Pharmacology and Experimental Therapeutics
University of Mississippi

William C. Levin
Assistant Professor of Internal Medicine
University of Texas Medical Branch

Ralph W. Brauer
Assistant Professor of Biochemistry
Louisiana State University

Charles D. Van Cleve
Associate Professor of Anatomy
University of North Carolina

Joseph W. Beard, Professor of Surgery, in charge of Experimental Surgery
Duke University

COOPERATIVE ACTIVITIES

As noted earlier, one of the strong factors in locating the cancer research program here was the proximity of unique facilities and gifted staffs in chemistry, biology, physics, health physics, and related fields, and Dr. Brucer entered negotiations early for the use of these staffs and facilities. For instance, much of the animal work, especially that concerning large animals, will be carried out at the AEC-UT Experimental Farm in Oak Ridge. Contract negotiations are now under way to spell out the details of this arrangement.

A part of the research program in the field of pathology will be carried out in cooperation with facilities now being constructed at the Biology Division of Oak Ridge National Laboratory. On a more informal basis, the Medical Division is receiving invaluable assistance from the Isotopes Division of the Commission, and from the Health Physics, Chemistry and Physics Divisions of Oak Ridge National Laboratory.

Contract negotiations also are under way with the Oak Ridge Hospital's Board of Trustees concerning the use of certain hospital facilities in the medical program.

CONSTRUCTION

In January, a contract was drawn up with the Austin Engineering Company which called on the firm to prepare the necessary engineering and construction drawings and plans for the new hospital building, together with the re-modeling of the present "E" wing of the Oak Ridge Hospital.

The engineers estimates for the cost of the building program was around $340,000. Through a fortuitous series of events, most important of which was the sharp decline in construction costs in the Oak Ridge area, the total cost of the building will be $270,000. Bids were opened on June 16, and by the end of the fiscal year on June 30, Baskerville Builders, the successful bidders, already had done preliminary excavating and sunk footings for the new building. The contract allows the firm 240 calendar days to complete the project.

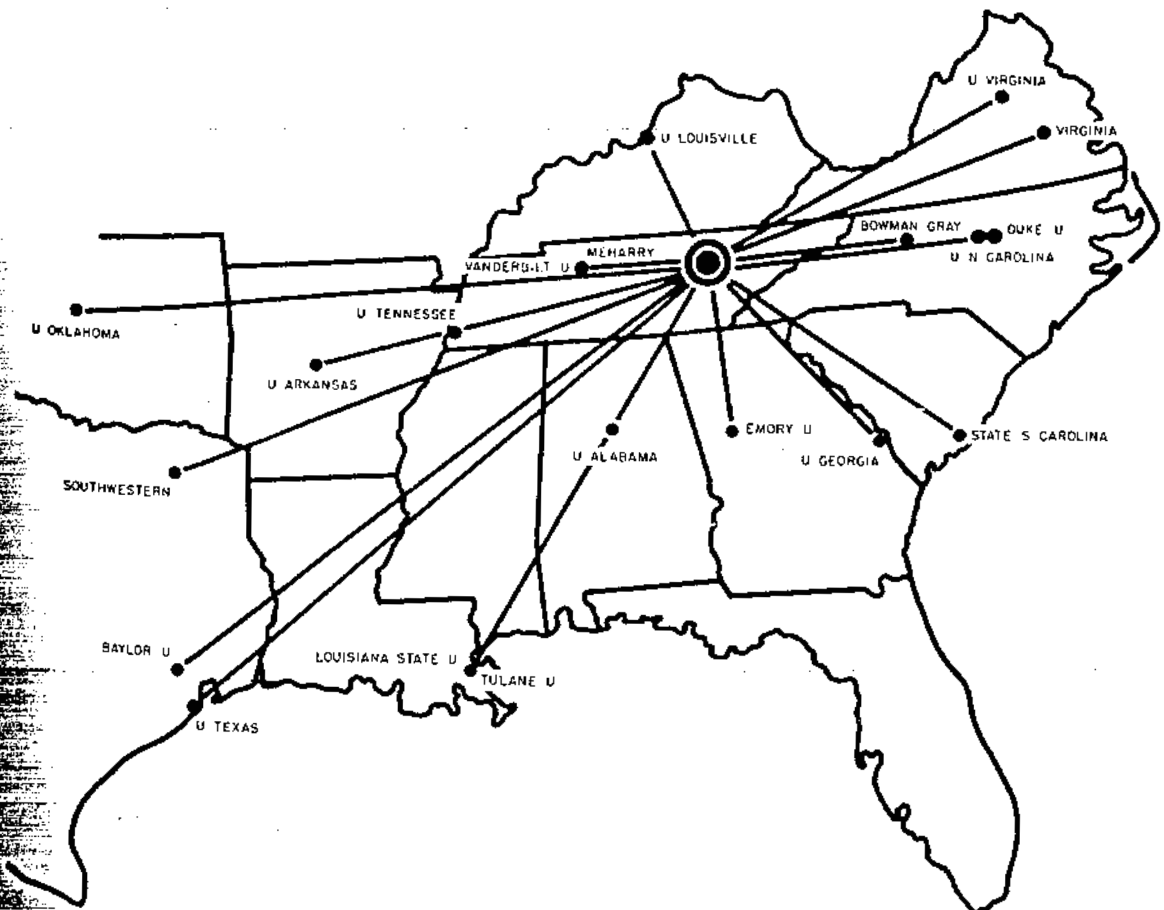
In the meantime, the Division has already established two laboratories in the present "E" wing to conduct preliminary studies.

CONSTRUCTION of the Institute's Cancer Research Hospital, shown in the above picture, began in June. The 30-bed unit is expected to be completed in March 1950.

COURSE FOR PRACTICING PHYSICIANS

With the establishment of the Medical Division of the Institute and of the University of Tennessee Memorial Hospital and Research Center in Knoxville, there was considerable demand among practicing physicians in the East Tennessee area for an orientation course in the use of radioisotopes in medical research. As a result, the Medical Division and the Special Training Division set up a demonstration and lecture course on the Usefulness of Atomic Energy in Medical Practice. The course consisted of eight sessions of one and one-half hours each on Wednesday and on Friday afternoons during the month of May. From a large number of applications, 59 physicians were registered for the course, which was given for informational purposes only and certainly was not presented as a course qualifying practitioners to use radioisotopes in research.

MEDICAL SCHOOLS



INSTITUTIONS PARTICIPATING

SCHOOLS PARTICIPATING IN MEDICAL PROGRAM

University of Alabama School of Medicine
Birmingham, Alabama

University of Arkansas School of Medicine
Little Rock, Arkansas

Baylor University College of Medicine
Houston, Texas

Bowman Gray School of Medicine
Winston-Salem, North Carolina

Duke University School of Medicine
Durham, North Carolina

Emory University School of Medicine
Atlanta, Georgia

University of Georgia School of Medicine
Augusta, Georgia

Louisiana State University School of Medicine
New Orleans, Louisiana

University of Louisville School of Medicine
Louisville, Kentucky

Meharry Medical College
Nashville, Tennessee

University of North Carolina Medical School
Chapel Hill, North Carolina

University ofOklahoma School of Medicine
Oklahoma City, Oklahoma

Southwestern Medical College
Dallas, Texas

State of South Carolina Medical College
Charleston, South Carolina

The University of Tennessee School of Medicine
Memphis, Tennessee

University of Texas--Medical Branch
Galveston, Texas

Tulane University School of Medicine
New Orleans, Louisiana

Vanderbilt University School of Medicine
Nashville, Tennessee

The Medical College of Virginia
Richmond, Virginia

University of Virginia School of Medicine
Charlottesville, Virginia

6/30/50

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Fourth Annual Report

of the

Oak Ridge Institute of Nuclear Studies

June 30, 1950

Operating Under Contract

With the

UNITED STATES ATOMIC ENERGY COMMISSION

VII

Medical Division

THE MEDICAL Division of the Institute was established to furnish the participating Southern medical schools with facilities at Oak Ridge for study of neoplastic diseases through the exceptional research tools available there. The program had its genesis in a request by the Atomic Energy Commission made in January, 1948, that the Institute consider the feasibility of operating such a program. The Institute then asked each Southern medical school to send a representative to a conference in Oak Ridge on March 1 and 2, 1948, to advise on the feasibility of the program and if approving, to establish its broad outlines. Within this framework, the Board of Medical Consultants of the Institute, established at the suggestion of the March conference, laid out the detailed program during the last six months of 1948. The Division Chairman, Dr. Marshall Brucer, began work on December 30, 1948, and immediately launched into the myriad problems incident to establishing a 30-bed hospital, assembling a staff, and initiating the program.

RESEARCH PROGRAM

The basic plan for the Medical Division includes a central research program and peripheral training, information and special project activities carried out in cooperation with the staffs of the participating medical schools. All four of the programs center around the use of isotopes in the study of neoplastic diseases, with the central program being the investigation of the value and use of isotopes in the biology and therapy of neoplasia.

Preliminary to the beginning of effective research was the problem of designing and constructing a hospital and accompanying laboratories, the bringing together of research, medical, nursing, and administrative staffs, the construction of shops and the establishment of suitable animal facilities. While only a few months of actual laboratory work was accomplished during the year, progress was such as to allow the Division to accept its first patient a month before the building to house the program was completed. Major accomplishments during the year were as follows:

a. The 30-bed research hospital and laboratory building was constructed and placed in operation.

b. The nursing staff was assembled and given necessary training in health physics and in the management of patients with radioactive injections.

c. The medical staff, technicians and administrative staff had set up procedures to obtain patients and operate the hospital unit.

d. Liaison was established with the participating medical schools as to types of patients, numbers, procedures and legal aspects of the program.

e. A small number of patients were accepted in the hospital requiring already well-standardized radioactive treatments in order to establish general administrative procedures.

f. An animal colony with necessary equipment, yards and adjacent experimental laboratory was completed in cooperation with the UT-AEC Agricultural Research Program.

As noted above, the first patients accepted by the Division were those afflicted with diseases for which there was already an established backlog of experience in the therapeutic use of radioisotopes. This policy was followed in order to establish treatment procedures. Too, additional preliminary work was required before new radioisotopes could be used in treatment. However, the nature of the program is such that the major energies of the staff will be devoted to investigating new types of isotope treatment. A number of those already planned are set out below.

GALLIUM

In addition to the use of radioactive phosphorus, sodium, gold, and iodine, the Division is making a searching investigation of the possibilities of using radioactive gallium, a gamma and beta emitter, in treating bone cancers. Gallium is a rare metal occurring just above aluminum on the periodic chart of the elements. Work done by Commander H. C. Dudley, of the Navy Medical Corps at Bethesda, Md., indicated that gallium showed preferential concentration in bone, particularly in rapidly growing bone and callous. As such, it may be of value in treating osteoblastic bone both primary and metastatic, and in particular, the metastases from prostatic carcinoma. Considerable animal work has been done to determine toxicity values, excretion patterns, and other data. A concurrent line of investigation concerns the design of instruments for injection of gallium, the preparation of suitable gallium-containing biological salts, related problems of biochemistry and other aspects of the use of this radioisotope in cancer therapy.

RUTHENIUM

Another radioactive isotope under consideration is Ruthenium 106, which emits two strong beta particles in decaying, with relatively little gamma radiation. Such an isotope makes possible relatively intense local surface irradiation, and as such ruthenium is of interest to a number of dermatologists in the participating medical schools. The cancer committee of the University of Tennessee College of Medicine has been particularly interested in this isotope, and Dr. Joseph Cata, senior resident in radiology, was the Medical Division's first resident. He studied the design of a collimating ... apparatus to determine depth dosage and distribution. Plaques and applicators of various designs will be tested on animals. Other radiology groups are interested in the use of ruthenium applicators to determine the specific effect of high radiation dosage on certain tissues.

Considerable additional experimental work remains to be done with ruthenium, since there is ... pertinent material in the literature on distribution and toxicity. Ruthenium behaves as a noble metal and since the chemistry of the element is little known, it will be necessary to find a stable salt of the metal which will not deposit locally or form a colloid. Results to date show a formation of ... of deposited material with a very slow ... into the general circulation. Ruthenium can be plated on objects of almost any form which can be employed as a surface applicator and ... to apply localized radiation. The possibility of treating neoplastic tissue or metastases by ... term local implantation in areas not available ... ally will be investigated. A long half-life ... use of ruthenium internally.

COBALT

The radioactive isotope of cobalt (cobalt 60) ... to hold unusual promise in the radiation treatment of deep-seated tumors. As a result, the Medical Division and the M.D. Anderson Hospital for Cancer Research at Houston, Texas, are cooperating in the designing, building and testing of a 1,000-Curie radiocobalt teletherapy unit. A building is now under construction adjacent to the Medical Division building in Oak Ridge for housing the unit during tests. When all test phases are completed, the unit if satisfactory will be sent to the M.D. Anderson Hospital for therapeutic use.

Radiocobalt is a hard gamma ray emitter with a half-life of about five years. It is believed to have advantages over both radium and x-ray radiation in cancer therapy. It is cheaper than radium, easier to handle, and great amounts of activity can be concentrated into small amounts of the metal. Cobalt produces a monochromatic ... which may be directed to deep-seated locations within the body. X-rays used in this manner often produce serious skin burns due to the variable wave length, without appreciable therapeutic effect.

Dr. Leonard G. Grimmett, a British physicist now on the M.D. Anderson Hospital staff, designed the unit. A 200-Curie sample of cobalt for testing already has been allocated. The final sample of 1,000 Curies probably will be irradiated at the higher flux reactor in Chalk River, Canada.

The radiocobalt unit is the first of its kind to be authorized by the Atomic Energy Commission.

MANGANESE

Recent studies of the distribution of manganese in the body suggest a transient selective localization in the thyroid. This effect is being studied in animals using cyclotron-produced radioactive manganese, and if results warrant, additional studies leading toward use of the metal in man will be carried out.

HEMATOLOGICAL AGENTS

Neostibosan, a compound containing antimony, has been reported to exert a favorable effect in multiple myeloma. A number of hematology groups in the medical schools are interested in this problem, and Dr. Carl T. Bahner, a consultant to the Medical Division, is interested in synthesizing the drugs with labeled antimony. If this can be done, observation will be made as to whether the drug enters the atypical plasma cells, particularly during the formation stages in the marrow. If there is a selective pickup, radioactive antimony may increase the effectiveness of this drug.

FOLIC ACID STUDIES

The Division is planning to study the metabolism of folic acid and folic acid antagonists in leukemia. Dr. Howard Skipper, of the Southern Research Institute, has reported that he believes it possible to attach radioactive atoms to the para aminobenzol acid ring in folic acid compounds with a considerable degree of stability. Such compounds would be expected to behave physiologically like those without the label, although these assumptions must be carefully tested.

TRAINING PROGRAM

The Medical Division contains some of the most advanced facilities in the country for investigating the value of radioisotopes in cancer therapy, hence a training program is second in importance to the research program and is in fact a vital part of it. To this end, arrangements have been completed for the acceptance of senior residents of the participating medical schools for periods of three months. These residents are of two types. Where no specific research program is planned, the resident will be given training in the use of isotopes already approved for use in human patients. They will be given instruction in the use of measuring, monitoring, and safety devices and will follow the clinical course of the patients under treatment. The other type resident is one who comes to work on a specific research problem carried out cooperatively by the Medical Division and the school in question.

The Institute is also able to grant research fellowships in certain cases so that medical school personnel can come to the Division for three months of research participation and training. Plans are also being developed to allow medical school personnel to work with the Division staff for shorter periods of time.

INFORMATION PROGRAM

An essential part of the Division will be the ready dissemination of worthwhile information developed on the project. To date this has consisted largely of providing information on building and laboratory design for radioisotope use. A number of architects and medical school representatives have received such data. Members of the Division staff have provided considerable information to manufacturers of fume hoods and other laboratory furniture to assist them in designing equipment needed for radioisotope work. Considerable information has been provided medical schools concerning instrumentation problems in newly-designed radioisotope laboratories.

The major information activity will concern research results when they become known. In the meantime, members of the staff have given a large number of addresses to various medical groups in the South. These have largely concerned the medical aspects of atomic energy and the use of radioisotopes in medical research. Dr. Brucer, Division Chairman, spoke at the Fourth Annual Cancer Symposium in Houston, the Hematology Conference of the American College of Surgeons in Birmingham and at meetings of the American Cancer Society in Nashville, the Alpha Omega Alpha fraternity in Memphis, University of Georgia Medical School, University of Mississippi, University of Texas, Bowman Gray School of Medicine, and Louisiana State University.

Dr. H. D. Bruner addressed the Civilian Radiological Teacher Training Course, the Oak Ridge Naval Reserve Research Group and the Federated Society Meetings at Atlantic City. He delivered a series of three lectures in his capacity as Visiting Professor of Pharmacology at the University of North Carolina School of Medicine and gave a paper at Duke University.

Dr. J. D. Perkinson of the Medical Division gave a paper at the meeting of the American Physiological Society and delivered lectures in the Radioisotope Training Program, and to the Naval Research and Civilian Radiological Training Program.

SPECIAL PROJECTS

An important part of the medical problem w be the admission of staff members of the participat medical schools to the Oak Ridge facilities special projects which cannot be undertaken at medical school. The first such proposal already been received from the Physiology Departm of the University of Tennessee College of Medic

CONSULTANTS

The complexity of modern cancer research the newness of the present approach assumes small permanent staff with a much larger group consultants from the medical schools to assist the program. This consultant staff, which consists of 65 individuals, is organized to in active participation by the cooperating medi schools--an essential for the Division to functi properly--and to bring into the program medi scientists from outside the region whose tale will prove uncommon assets to the Division. T consultant staff has been a major factor establishing effective liaison with the medi schools.

The clinical hospital unit and attac research laboratories and treatment rooms is first unit to be designed specifically for the use atomic energy projects in medicine. Very spe problems are involved here which will bec commonplace problems in hospitals if radioacti materials prove generally useful in therape work. For instance, attention to a single pati rarely would subject physicians and nurses serious radiation exposure; on the other ha the cumulative effect of attending several patie with radioactive injections may create a serio hazard. The disposal of radioactive wast creates another special problem, as does t disposal of radioactive gases in quantity fr hoods, particularly in view of the fact that m hospitals are located in heavily-populated sectio Storage and handling of a variety of radioisotop to be used clinically present considerable proble The fact that it is the first unit to be so design together with the position of Oak Ridge as center of information on and production of radi active materials, places certain responsibiliti on the Medical Division in the way of design a use of the facilities.

Some of the ways in which the Medical Divis has approached these problems are:

a. Members of the Division staff have gone manufacturers of laboratory equipment and assi in the design of satisfactory hoods for radioiso work in medical installations. Such hoods have be installed in the research laboratories and operating room of the Division.

b. Four 4,000-gallon settling tanks have be installed for the collection of radioactive wa Research laboratories, washing facilities, and

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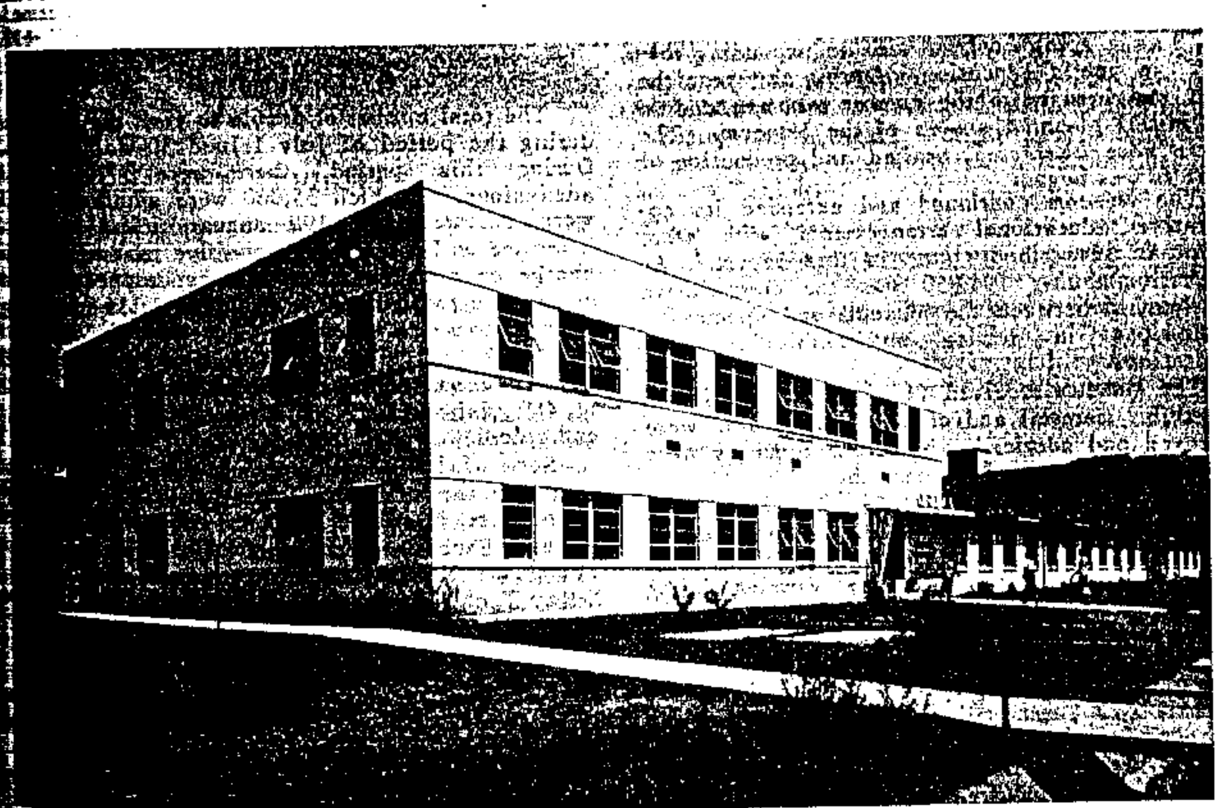
other units where radioactive wastes are involved are connected directly to these tanks, which hold the waste until the radioactivity is of a low enough level for normal disposal.

c. Special techniques are being developed through animal experimentation for injecting radioactive materials.

d. A well-designed, inexpensive radiation storage vault has been built into the unit.

e. Special air outlets containing filters developed by the Army Chemical Corps have been installed in the flues to collect gases from the hoods.

f. All standard monitoring procedures, such as film badges, pocket meters, survey meters and the like are in effect.



APPENDIX V

MEDICAL DIVISION

I. Board of Medical Consultants

George T. Harrell	Bowman Gray Sch. of Medicine
Vernon W. Lippard	University of Va. Med. Dept.
Robert M. Taft	Med. Col. State of S. C.
Douglas H. Sprunt	Univ. of Tenn. Sch. of Med.
Wilburt C. Davison	Duke University
*Roy.R. Kracke	Med. Coll. of Alabama

*Deceased

II. Special Consultants

Francis Chambers	Army Medical Research Inst.
Eugene Cronkite	Army Medical Research Inst.
John Tullis	Army Medical Research Inst.
Horace C. Dudley	U. S. Navy, Bethesda, Md.
E. Richard King	U. S. Navy
Douglas Baldridge	Univ. of Penna. Sch. of Med.
Harvey Blank	Univ. of Penna. Sch. of Med.
Carl T. Bahner	Carson-Newman College
Harry D. Bruner	University of N. C. Sch. of Med.
James C. Drye	Univ. of Louisville Sch. of Med.

III. Liason Consultants in Participating Medical Schools

Baylor Univ. School of Medicine	Joseph Gast
Bowman Gray School of Medicine	Jerry K. Aikawa
	John R. Andrews
	Camillo Artom
	Clyde T. Hardy, Jr.
	Reid T. Holmes
	Charles Norfleet, Jr.
	Ernest W. Yount, Jr.
Duke Univ. School of Medicine	Joseph W. Beard
	Clarence Gardner
	Philip Handler
	Jerome S. Harris
La. State Univ. Sch. of Medicine	Ralph W. Brauer
Med. College of the State of S.C.	Raymond Postlethwait
Med. Dept. of the Univ. of Va.	Kenneth R. Crispell
	H. Rowland Pearsall
Medical College of Alabama	John M. Bruhn
	Robert Teague
Univ. of Ga. Sch. of Medicine	Stephen W. Brown
	Hoke Wammock
	Henry L. Schmidt, Jr.
Univ. of Kansas Sch. of Med.	Paul Schafer
	Galen M. Tice
Univ. of Louisville Sch. of Med.	James T. Brad
	James C. Drye
	R. Arnold Gri
	Herbert D. Ke
	Hampden C. L
	James M. Kin
	Everett L. Pirk
	David Shapiro
Univ. of Miss. School of Med.	Arthur C. Guyt
University of North Carolina	Arthur Roe
	Charles Van C
Univ. of N. C. School of Med.	Edward M. Hed
	Cornelius T. K
	William G. Mor
Southwestern Univ. Sch. of Med.	Allen F. Reid
Univ. of Tennessee Sch. of Med.	Lester Van Mid
	John L. Wood
	David S. Carroll
	Alys H. Lipsc
	Carl E. Nurnbe
	Robert A. Wood
Univ. of Texas Sch. of Medicine	Charles R. Alle
	Ludwick Anig
	R. Lee Clark, J
	Gilbert H. Flet
	Leonard G. Gri
	S. Grant Holmes
	Kenneth P. McC
	Howard G. Swa
Vanderbilt Univ. Sch. of Med.	Howard J. Curti
	Herbert C. Fra

IV. Resident Physicians

Dominic Joseph Cara	Univ. of Tenn. Med. Sch.

V. Nursing Staff

Mary Sutliff
Vivian Gruenwald
Freda Schukofski
Roberta Clouser
Frances Sanderson
Mary Miller
Verda Wells

APPENDIX VI

MUSEUM

I. Technicial Advisory Committee

Paul C. Aebersold	Atomic Energy Commission
Gould A. Andrews	OR Inst. of Nuclear Studies
Cyril Comar	UT - Ag. Res. Prog.
Joseph A. Conners	K-25
Donald D. Cowen	N.E.P.A.
Logan B. Emlet	Oak Ridge National Lab.
Leo F. Hemphill	Y-12
Richard F. Kimball	Oak Ridge National Lab.
R. L. Macklin	K-25
Edward McCrady	Atomic Energy Commiss
Edgar J. Murphy	Oak Ridge National Lab.
A. L. Rydzewski	Atomic Energy Commiss
C. D. Susano	Y-12
F. Western	Oak Ridge National Lab.
Edwin A. Wiggin	Atomic Energy Commiss

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Consultants

Harry E. Wheeler	Cherokee Indian Museum
Jerome K. Kuderna	Alabama Polytechnic Inst.
W. J. McGlothlin	Bd. of Control, Sou. Reg. Educ.
Maurice F. Seay	University of Kentucky
William T. Clifford	Sou. Educ. Film Prod. Ser.
James E. Arnold	University of Tennessee

AEC, Oak Ridge, Tenn. 11-3-50-2000-A7766

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OAK RIDGE INSTITUTE OF NUCLEAR STUDIES

FIFTH

ANNUAL REPO

for the year ending JUNE 30, 1

in which bone involvement is present and is the main cause of symptoms.

4. Pleural metastases from any type of neoplasm in which recurrent pleural effusion is the main problem, preferably without massive intrapulmonary lesions.

5. Carcinomatosis of the abdomen without obstruction of the urinary or gastro-intestinal tract and in which ascites is the main cause of symptons.

6. Carcinoma of the thyroid not amenable to surgical therapy.

7. Active Hodgkins disease previously treated, but for which there is no known satisfactory treatment.

8. Multiple myeloma.

9. Chronic myelocytic leukemia.

10. Polycythemia vera.

TRAINING PROGRAM

As in any other medical program, the best training is active participation in the clinical and research program. Consequently, except for taking the basic radioisotope techniques courses given by the Special Training Division, no formal training is given residents. They form an invaluable part of the clinical program and also participate in the research program.

RESEARCH PROGRAM

The use of any new isotope in medical therapy requires exhaustive research in the laboratory and in animals. The Medical Division is one of the few organizations prepared to carry a study from the idea stage, through the chemical preparation of materials for the reactor or cyclotron, biological preparation after irradiation, through toxicity studies, distribution studies, excretion patterns, preparation and testing of suitable biological compounds, the use of tracer quantities in humans, and finally to therapeutic testing. The major radioisotopes tested or used during the year are discussed in the following sections.

GALLIUM

As noted in the 1949-50 Annual Report, one of the first studies undertaken by the Medical Division involved the use of radioactive gallium in treating bone cancer of the osteoblastic type, both primary and metastatic in nature. This study was undertaken because gallium concentrates selectively in areas of bone growth and destruction.

While the clinical results of treatment have not been encouraging in most cases, neither have they been sufficiently discouraging to cause a slackening of effort. Twenty-two patients have received therapeutic doses of gallium, and another 29 have received tracer doses.

Considerable research in animals was carried out during the year in connection with the use of gallium, and at the year's end one of the major difficulties of gallium therapy seemed near a solution. Gallium-72, the reactor-produced radioisotope, is present in relatively small quantities along with much larger amounts of stable Gallium-69-71. Since the material acts as a cumulative poison, the amount of radiation that can be brought to bear against a tumor is limited by the toxicity of the metal. Gallium-67 is now being produced by bombarding zinc in the Oak Ridge cyclotron. It can be separated chemically from the zinc and thus will be a relatively pure radioisotope, allowing much higher dosages to be given. This material is not yet available for use in patients, since considerable animal work must be carried out to determine what compounds are suitable for therapeutic use.

GOLD

The use of radioactive gold in intractable pleural and peritoneal effusion arising from neoplasia has shown encouraging clinical results. Gold is a short-range beta and gamma emitter. In its colloidal state, it does not circulate throughout the body but remains well-localized in the cavity or area in which it is injected, there delivering a heavy radiation dose to a restricted area.

A wide variety of studies were carried out in animals to determine the characteristics of radiogold, and later in the year these studies were extended to humans. The use of radiogold will be a major clinical activity during the coming year.

In addition to being of interest clinically, radiogold has turned out to be an excellent teaching radioisotope. It is readily available, easy to obtain, can be measured in very small or very large doses, is sufficently long-lived (2.7 days) for slow, meticulous work and yet is sufficiently short-lived to minimize the contamination hazard. This material is being used in a large number of medical installations.

ANTIMONY

A trivalent organic complex of antimony has been studied in a number of normal rats. High concentrations in the red cells and in the liver were noted. Antimony also showed high concentration in tumor cells of five types of mouse tumors. The study has been extended to the in May of Dr. Leonard G. Grimmett, physicist M.D. Anderson Hospital who designed the and was a world leader in radium beam y.

DEXTRAN

The Division is making its facilities available Emory University Medical School, which is ...ting an extensive study of dextran, a ...e polymer which seems to have excellent ...ilities as a blood volume expander. Certain ... of the work which utilized Carbon-14 ... techniques could not be carried out at ... and arrangements were made under which could be carried out at Oak Ridge. Dr. Cargill, a member of the Emory University ...ment of Physiology, is conducting the Ridge phase of the investigation.

HEMATOPORPHYRINS

...published article by Dr. F. H. J. Figge and ...iates at the University of Maryland Medical ... on the specific localization in tumors of ...oporphyrin and zinc-hematoporphyrin (deriva... of the hemoglobin of the blood) led to the ...tion that it be used therapeutically. A ... of experiments on tumor-bearing mice using ...oporphyrin were carried out to check this ... Examined under ultra-violet light, the ... did fluoresce more than normal tissues, ...ing the findings of the article, but chemical ... of the compound have failed to show the ...ation indicated by the fluorescence. Why ... tissue intensifies the fluorescence con... an interesting lead in tumor biology.

AUTORADIOGRAPHY

Autoradiography gives promise of being an exceptionally strong diagnostic tool and considerable attention is given to it in the Division.

A gross autograph technique has been developed and has become a routine method. It is purely qualitative, and work continues on quantitation of gross autograms. Work is underway on micro-autoradiographic techniques and interpretation.

Autoradiographic studies are being applied to such problems as radiocolloid distribution in relation to surface properties of colloids, localization of formate carbon in leukemic blood cells, and sulfur-labeled methionine in myeloma cells. Methods are being developed for external autoradiography in humans.

About half of the autoradiography program is concerned with service investigations for other members of the staff.

STAFF ACTIVITIES

Members of the staff of the Medical Division made 97 talks during the year before medical, scientific and lay groups. In the early days of the program, all requests for speakers were honored, but the number of requests has grown so large that at the present time a number must be refused.

Fifteen formal papers have been presented to societies and either have been accepted for publication or allied work is being prepared for publication.

Jean Thomas	Receptionist
Thomas	Maintenance Mechanic II
W. Triplett	Maintenance Mechanic II
E. Vail	Record Clerk
L. Vaughn	Chief Maintenance Mechanic
L. Vaughn	Delivery Man
M. Walker	Instrument-maker
Dudley Walker	Instrument-maker
Wallace	Cabinet-maker
Wilde	Instrument Engineer
Williams	Helper

OFFICE OF BUSINESS MANAGEMENT

J. W. Mumford, Business Manager

B. Brown	Secretary
G. Disney	Accounting Clerk
Mae Holloway	Clerk-typist
McCallum	Bookkeeper
McGill	Accountant
N. Nanney	Accounting Clerk
Rose, Jr.	Head, Accounting Department
Rutherford	Auditor

UNIVERSITY RELATIONS DIVISION

Russell S. Poor, Chairman

T. Clark	Assistant, Univ. Rel. Division
Clouse	Clerk-typist
Dryden	Administrative Assistant
Francis	Stenographer
Hobbs	Stenographer
Mae Holtzclaw	Clerk-typist
H. Prater	Clerk-typist
Rowe	Secretary
Strange	Administrative Aide

MEDICAL DIVISION

Marshall Brucer, Chairman

A. Andrews	Chief, Clinical Service
Claire Bondurant	Laboratory Technician
A. Boyd	Senior Scientist
D. Bruner	Chief Scientist
R. Buher	Laboratory Technician
Peter Byrom	Health Physicist
Cantrell	Laboratory Technician
Carden	Stenographer
H. Cargill, Jr.	Research Assistant
A. Carpenter	Custodian
Louise Cook	Receptionist
Ray Cooper	Laboratory Technician
Marguerite Cooper	Senior Scientist
Allen Cress	Laboratory Technician
C. Dixon	Laboratory Aide
Dobson	Helper
S. Edwards	Receptionist
S. Eldridge	Research Technician
Gallimore, Jr.	Research Assistant
Gray	Research Associate
Albert Greene	Laboratory Technician
Harmon	Administrative Assistant
L. Hayes	Associate Scientist
Mary Ann Heppert	Laboratory Technician
Eva E. Hodgens	Laboratory Technician
Herbert D. Kerman	Radiologist
Priscilla A. Oliver	Occupational Therapist
Dorothy G. Osteen	Secretary
Jesse D. Perkinson	Senior Scientist
Samuel W. Root	Assistant Clinician
Robert Sellers	Research Technician
William Smith, Jr.	Laboratory Technician
Frieda R. Urey	Laboratory Technician
Alice H. Whitson	Medical Records Librarian
G. Curtis Wilson	Research Technician

SPECIAL TRAINING DIVISION

Ralph T. Overman, Chairman

Walter Clossey	Audio-Visual Technician
Ralph Henry Firminhac	Scientist
Rex G. Fluharty	Senior Scientist
Walter E. Graves	Laboratory Technician
Iziah Jones	Custodian
Elizabeth Rona	Senior Scientist
Frances E. Smellage	Secretary
Donald R. Smith	Associate Scientist
William Donald Wallace	Laboratory Assistant
Edith Wilson	Secretary

MUSEUM DIVISION

David L. DeJarnette, Chairman

Margaret M. Abdian	Secretary
Carolyn M. Bradford	Museum Aide
Lennie A. Childress	Stenographer
W. Earl Duff	Museum Assistant
Jean E. Fahey	Receptionist
Wheeler Fain	Custodian
Renfro Henderson	Custodian
Basil Martin	Curator
Theodore J. Robbins	Helper
Donald G. Robertson	Museum Assistant
Robert C. Rothermel	Museum Aide
Lawrence Sharp	Preparator
Andrew C. Smith	Museum Aide

TERMINATIONS

OFFICE OF THE EXECUTIVE DIRECTOR

Robert A. Burgin, Jr.	Public Information Specialist

OFFICE OF ADMINISTRATION

H. D. Beck, Jr.	Head, Management Servs. Dept.
A. H. Frost, Jr.	Head, Services and Supply
Thomas C. Giles	Maintenance Mechanic I
Elizabeth K. Hinton	Stenographer
Harold F. Holzer	Instrument Maker
Mary L. Patterson	Stenographer
Jack D. Queener	Junior Clerk
John J. Roberts	Instrument Maker
Anne P. Strunk	Clerk-typist
Lawrence Swinford	Maintenance Mechanic
Orville R. Swinford	Maintenance Mechanic

Morris E. Rose	ORNL
Arthur H. Snell	ORNL
E. O. Wollan	ORNL

VII. AEC-Predoctoral Fellowship Board

George B. Pegram, Chm.	Columbia University
George H. Boyd	University of Georgia
Robert B. Brode	University of California
Detlev W. Bronk	The Jouhs Hopkins Univ.
Leland J. Haworth	Brookhaven National Lab.
Warren C. Johnson	The University of Chicago

VIII. Radiological Physics [illegible]

E. E. Anderson	ORNL
W. D. Claus	AEC
R. A. Patterson	Brookhaven Nat'l Lab.
H. M. Roth	AEC
F. G. Slack	Vanderbilt
J. N. Stannard	University of Rochester
R. S. Poor	ORINS

APPENDIX III

MEDICAL DIVISION

I. Medical Advisory Panel

R. Lee Clark, Jr.	M.D. Anderson Hospital
Wilburt C. Davison	Duke University
George T. Harrell	Bowman Gray School of Med.
Hayden C. Nicholson	University of Arkansas
Vernon W. Lippard	University of Virginia
Douglas H. Sprunt	University of Tennessee

II. Consultants to Medical Division

Jerry K. Aikawa	Bowman Gray Sch. of Med.
Charles R. Allen	Univ. of Texas Med. Branch
John R. Andrews	Bowman Gray Sch. of Med.
Ludwik Anigstein	Univ. of Texas Med. Branch
Camillo Artom	Bowman Gray Sch. of Med.
Paul C. Aebersold	Atomic Energy Commission
Carl T. Bahner	Carson Newman College
Joseph W. Beard	Duke Univ. Sch. of Med.
Harold F. Berg	Univ. of Louisville Sch. of Med.
Harvey Blank	Univ. of Pa. Sch. of Med.
Walter L. Bloom	Emory Univ. Sch. of Med.
Ralph R. Braund	Univ. of Tenn. College of Med.
Stephen W. Brown	Georgia Sch. of Med.
David S. Carrol	Univ. of Tenn. College of Med.
Francis W. Chambers	Naval Med. Research Inst.
William E. Cornatzer	Bowman Gray Sch. of Med.
Kenneth R. Crispell	Univ. of Virginia
Eugene P. Cronkite	Naval Med. Research Inst.
James C. Drye	Univ. of Louisville Sch. of Med.
H. C. Dudley	Naval Med. Research Inst.
H. H. Dunham	Univ. of Kansas Med. Center
George A. Emerson	Univ. of Texas Med. Branch
Gilbert H. Fletcher	M.D. Anderson Hospital, Houston
Herbert Francis	Vanderbilt Univ. Sch. of Med.
Robert W. Gardier	Univ. of Tenn. College of Med.
Clarence E. Gardner	Duke Univ. Sch. of Med.
Joseph Gast	Baylor Univ. Sch. of Med.
R. Arnold Griswold	Univ. of Louisville Sch. of Med.
Arthur C. Guyton	Univ. of Miss.
William F. Hamilton	Univ. Hospital, Augusta, Ga.
Philip Handler	Duke Univ. Sch. of Med.
Clyde T. Hardy	Bowman Gray Sch. of Med.
Jerome S. Harris	Duke Univ. Sch. of Med.
William N. Harsha	Univ. of Kansas Med. Center
Edward M. Hedgpeth	Univ. of North Carolina
Robert Hetting	Baylor Univ. Sch. of Med.
S. Grant Holmes	Univ. of Texas Med. Branch
Reid T. Holmes	Bowman Gray Sch. of Med.
Margaret W. Holt	New England Deaconess Hosp.
Coleman Jacobson	Univ. of Pennsylvania
Cornelius T. Kaylor	Univ. of N. C. Sch. of Med.
E. R. King	U. S. Naval Hospital, Bethesda
J. Murray Kinsman	Univ. of Louisville Sch. of Med.
Charles F. Kittle	Univ. of Kansas Med. Center
Hampden C. Lawson	Univ. of Louisville Sch. of Med.
William C. Levin	Univ. of Texas Med. Branch
Alys H. Lipscomb	Univ. of Tenn. College of Med.
Champ Lyons	Med. College of Univ. of Ala.
Kenneth P. McConnell	Univ. of Texas Med. Branch
Walter H. Mendel	Kennedy VA Hospital, Memphis
George R. Minor	Univ. of Virginia Hospital
William G. Morgan	Univ. of North Carolina
Franklin Murphy	Univ. of Kansas Sch. of Med.
Charles M. Norfleet	Bowman Gray Sch. of Med.
William E. Nunnery	Univ. of Tenn. College of Med.
Carl E. Nurnberger	Univ. of Tenn. College of Med.
H. Rowland Pearsall	Univ. of Va. Sch. of Med.
Elbert L. Persons	Duke Univ. Sch. of Med.
Everett L. Pirkey	Univ. of Louisville Sch. of Med.
R. W. Postlethwait	Med. College of South Carolina
Francis E. Ray	Univ. of Fla.
Allen F. Reid	Southwestern Med. College
Arthur Roe	Univ. of North Carolina
Wayne Rundles	Duke Univ. Sch. of Med.
Paul W. Schafer	Univ. of Kansas Med. Center
Henry L. Schmidt	Univ. of Georgia Sch. of Med.
S. M. Seidlin	Montefiore Hospital, New York
David Shapiro	Louisville VA Hospital
William W. Shingleton	Duke Univ. Sch. of Med.
Ralph W. Stacy	Ohio State Univ.
Kingsley M. Stevens	Lynchburg, Va.
Howard G. Swann	Univ. of Texas Med. Branch
Robert S. Teague	Univ. of Ala. Med. College
Galen M. Tice	Univ. of Kansas Sch. of Med.
John Tullis	Naval Med. Center
Charles Van Cleave	Univ. of North Carolina
L. Van Middlesworth	Univ. of Tenn. College of Med.
Hoke Wammock	Univ. of Georgia Sch. of Med.
Daniel T. Watts	Univ. of Virginia Med. School
Alfred E. Wilhelmi	Emory Univ. Sch. of Med.

George Z. Williams	Med. College of Virginia
Robert L. Woodbury	Univ. of Tenn. College of Med.
Ernest A. Yount	Bowman Gray Sch. of Med.

III. Research Participants

James W. Archdeacon	University of Kentucky
Betty M. Cooper	Univ. of Texas Med. Branch
Walter H. Cargill	Emory University
Robert S. Ingols	Georgia Institute of Tech.
Etta M. Macdonald	Univ. of Texas Med. Branch
Bert Nash	Univ. of Texas Med. Branch
John L. Wood	Univ. of Tenn. Col. of Med.

IV. Resident Physicians

Ferdinand Barnum	Bowling AF Base
Harold F. Berg	Univ. of Louisville Med. Sch.
Earl Evans Brant	Youngstown (Ohio) Hosp. Ass'n.
Dominic J. Cara	Univ. of Tenn. Col. of Med.
John F. Dillion	Randolph AF Base
Henry Howard Dunham	Univ. of Kansas Med. Center
Robert W. Gardier	Univ. of Tenn. Col. of Med.
William N. Harsha	Univ. of Kansas Med. Center
Roderick J. Humphreys	Univ. of Texas Med. Branch
E. R. King	U. S. Naval Hospital
Charles F. Kittle	Univ. of Kansas Med. Center
Lester E. Lutes	Carswell AF Base
John J. McKeown, Jr.	Nellis AF Base
Hugh McManus	March AF Base
William E. Nunnery	Bowman Gray Sch. of
Robert H. Owens	Univ. of Kansas Med.
R. K. Miller	Offitt AF Base
Donald Rathburn	Univ. of Texas Med.
Dana R. Schmidt	Henry Ford Hospital
Jack Schrader	Hamilton AF Base
Duane V. Sparks	Univ. of Kansas Med.
James M. Swain	Donaldson AF Base
Alonzo C. Tenney	Randolph AF Base
John E. Wear	Duke Univ. Sch. of M
Wesley Whitehouse	Barksdale AF Base
Walter K. Yates	Randolph AF Base

V. Nursing Staff

Mary Sutliff, Supervisor
Georgia Beets
Leona Boushka
Roberta Clouser
Gladys Cooper
Nell Craig
Bobbie Giovannuci
Juanita Johnson
Jean Leslie
Lucille Moran
Leah Murrin
Virginia Robison
Helen Smith

APPENDIX IV

SPECIAL TRAINING DIVISION

I. Consultants to Special Training Division

Herbert M. Clark	Rensselaer Polytechnic Inst.
Cyril L. Comar	University of Tennessee

II. Lecturers Assisting In Training Programs

Paul C. Aebersold	Atomic Energy Commission
Jerry Aikawa	Bowman Gray School of Medicine
Elda E. Anderson	Oak Ridge National Laboratory
M. Ashkenazy	VA Hospital, Houston
D. C. Bardwell	Oak Ridge National Laboratory
P. R. Bell	Oak Ridge National Laboratory
C. G. Borkowski	Oak Ridge National Laboratory
George A. Boyd	ORINS
G. E. Burch	Tulane Univ. Schl. of Medicine
David Cayre	Bowman Gray School of Med.
Cyril L. Comar	UT-AEC Research Program
Eugene Cornatzer	Bowman Gray School of Med.
Konrad Dobriner	Sloan-Kettering Institute
D. G. Doherty	Oak Ridge National Laboratory
E. Fairstein	Oak Ridge National Laboratory
C. A. Finch	Univ. of Washington Sch. of Med.
Gilbert H. Fletcher	M.D. Anderson Hospital, Houston
C. G. Goss	Oak Ridge National Laboratory
Paul F. Hahn	Meharry Medical College
George Harrell, Jr.	Bowman Gray School of Med.
Leon Hellman	Sloan-Kettering Institute
Alexander Hollaender	Oak Ridge National Laboratory
W. M. Hurst	Oak Ridge National Labo
L. O. Jacobson	University of Chicago
W. H. Jordan	Oak Ridge National Labo
F. R. Keating, Jr.	Mayo Clinic
S. Allan Lough	Atomic Energy Commission
Edward McCrady	Atomic Energy Commission
George Manov	Atomic Energy Commission
James Mason	Atomic Energy Commission
C. G. Montgomery	Yale University
Carl V. Moore	Washington Univ. Sch. of
R. J. Moon	University of Chicago
G. W. Morgan	Atomic Energy Commission
J. L. Morton	Ohio State University
Edith Quimby	Columbia University
Maurice S. Raben	New England Ctr. Hosp., Bo
R. W. Rawson	Memorial Hospital, N. Y.
J. F. Ross	Evans Memorial Hosp., Bo
Liane B. Russell	Oak Ridge National Labor
W. L. Russell	Oak Ridge National Labor
S. M. Seidlin	Montefiore Hosp., New York
F. R. Shonka	Argonne National Laboratory
John T. Storaasli	University Hosp. of Cleve
B. L. Vallee	Massachusetts Inst. of Tech
Don Ward	Atomic Energy Commission
Forrest Western	Oak Ridge National Labor
A. E. Wilhelmi	Emory University
John Wood	Univ. of Tenn. Sch. of Med
Paul Zemecnik	Massachusetts General Hosp

Radioisotope School Participants

Sixteenth Course

Victor E. Archer	U. S. Public Health Service
Harold E. Babbitt	University of Illinois
James P. Baker	Goldwater Memorial Hosp.,N.Y.
Stuart A. Bellin	University of Wisconsin
Thomas R. Blohm	Univ. of Texas Sch. of Dentistry
Louis E. Browning	Naval Radiological Defense Lab.
Clair J.Cavanaugh	University Hosps.,Okla.City
Donald J. Cook	DePauw University
Dean F. Davies	School of Medicine, Wash. Univ.
John M. Davis	Army Research & Dev. Lab.
E. A. Delwiche	Cornell University
David C. Gandy	Tenn. State College
Robert S. Ingols	Ga. Inst. of Technology
Theodore Kamholtz	Brooklyn, N.Y. Cancer Inst.
Justus G. Kirchner	La Canada, California
Herbert R. Lissner	Wayne University
T. A. Litovitz	Catholic University
James E. Miller	VA Hospital, Houston
Marion R. Myles	Tennessee State College
William E. Nunnery	Bowman Gray Sch. of Med.
James S. Reed	Naval Radiological Defense Lab. San Francisco
Grant L. Stahly	Ohio State University
Frederic E. Stynler	Ohio State University
David W. Talmage	Washington Univ. Sch. of Med.
Sol Taplits	Jewish Hosp., Cincinnati
Arthur W. Wase	Rutgers University
Orliss Wildermuth	New England Deaconess Hosp., Boston
Kent T. Woodward	Fitzimmons General Hosp., Denver
Waldo J. Younker	Kettering Lab., Cincinnati
Edward G. Zaino	Meadowbrook Hosp., N. Y.

Seventeenth Course

Johan Bjorksten	Bjorksten Res. Labs.,Madison
Albert L. Botkin	Field Res. Lab., Fort Knox,Ky.
Frederick J. Carleton	Purdue University
Roy M. Chatters	Oklahoma A&M College
Leland C.Clark, Jr.	Fels Res. Inst., Yellow Springs,Ohio
Frederic A. dePeyster	Presbyterian Hosp., Chicago
Charles R. Estee	University of South Dakota
Elwood G. Fisher	Cornell University
Kenneth A. Fry	University of Chattanooga
Carl E. Georgi	University of Nebraska
W. H. Goldwater	Tulane Univ. Medical School
Victor A. Greulach	University of North Carolina
Lloyd R. Hershberger	Shannon Memorial Hosp.,Texas
Coleman Jacobson	Univ. of Pa., Hospital
A. V. Jester	Bowman Gray Sch. of Medicine
E. L. Jones, Jr.	U.S.Naval Air Station,San Diego
Kazuo Kimura	St. Louis Univ. School of Med.
James W. Lewis	Colorado Springs Medical Ctr.
Frank M. Mateer	Univ. of Pittsburgh
Charles G. Miller	Univ. of California
Alfred P. Mills	Univ. of Miami
Llewellyn S. Mix	Univ. of Minnesota
Gerald M. Ridenour	Univ. of Michigan
Richard G. Roberts	Chicago Medical School
Morris Rockstein	State College of Washington
Arnold H. Schein	Univ. of Vermont College of Med.
Richard E. Schuster	State College of Mississippi
Elizabeth W. Smith	Kent Ohio State University
Virginia L. Sydow	Medical College of Georgia
Albert E. Taylor	Idaho State College
Leon W. Weinberger	Case Inst. of Technology
M. X. Zarrow	Purdue University
Robert E. Mack	St. Louis University
Byron W. St. Clair	Syracuse University

Eighteenth Course

Robert E. Bolinger	University of Kansas
Earl E. Brant	Youngstown Ohio Hosp. Asso.
Ann M. Budy	University of Chicago
Walter H. Cargill	Emory University
Alene W. Conover	Vanderbilt Univ. Hosp.
Robert J. Flipse	Pa. State College
L. M. Foster	Aluminum Res. Labs.,
Sheldon Fox	Bellevue Hosp., New York
Paul V. Freese	Johns Hopkins Univ.,Baltimore,
Robert W. Gardier	Univ. of Tennessee Med. Schl.
Herbert Isikow	U.S. Testing Co., Hoboken
Robert P. Gleason	Sylvania Elec. Products, Inc.,
Clarence G. Haupt	Norfold & Western Railway,
Samuel Helf	Picatinny Arsenal,Dover, N.J.
Frank L. Jackson	Procter & Gamble, Ivorydale,Ohio
Thomas F. Jackson	University Hospital, Augusta
Louis Laufer	Schwarz Labs., Inc., N. Y.
Jack Lehman	Physicians Hosp., N. Y.
LaVerne F. Lewis	USAF Institute of Technology
Robert C. Likins	U.S.P.H.S., Bethesda, Md.
William G. Long	University of Missouri
Allan L. Lorincz	University of Chicago Clinics
James L. McCoy	Revere Corp. of America, Conn.
John S. Nader	Environmental Health Center, Cincinnati
Paul Numerof	E. R. Squibb and Sons, N. J.
John M. Phillips	University of Pa. Hospital
Robert D. Ray	University of Washington
Francis X. Roser	Catholic University of Rio de Janeiro, Brazil
Charles A. Simkins	University of Idaho
Julius J. Smith	Graduate Hosp. of Univ. of Pa.
John H. Teeple	Marathon Corp., Rothschild, Wis.
Samuel B. Tove	N. C. State College

Nineteenth Course

John L. Bakke	Univ. of Washington Sch. of Med.
Jacob L. Beller	Hampton (Va.) Inst.
Milo E. Bixler	Hoover Co., North Canton, Ohio
Edward L. Breen	Engineering Division, USAF
Norman N. Breyer	Detroit Arsenal,North Canton,Ohio
Lucy M. Cavallo	National Bureau of Standards,
Ovle R. Czerwonka	Medical Dept. Field Res. Lab. Fort Knox, Ky.
Ruth E. Dunham	U. S. Public Health Service
Brooks M. Dusenbury	Maytag Co., Newton, Iowa
Thomas B. Gage	Univ. of Oklahoma Res. Inst.
Joseph D. Goldstein	U. S. Medical Corps

Allan L. Goulding	Billings (Mont.) Clinic
Gilbert Halverson	Fansteel Metallurgical Corp., Chicago
Robert J. Johnson	U. S. Medical Corps
Jacob Kastner	NRC of Canada, Ottawa
Joe R. Kimmel	Oakland (Calif.) Naval Hosp.
Melvin Levine	University of Michigan
D. S. McArthur	Standard Oil Development Co., Elizabeth, N. J.
James T. Penny	University of South Carolina
Charles S. Prince	Air Materiel Command, USAF
Cletis L. Roberson	Owens-Corning Fiberglas Corp., Newark, Ohio
Geraldine E. Secor	U. S. Dept. of Agriculture
Junius F. Snell	Charles Pfizer and Co., Inc., Brooklyn, N. Y.
Walter D. Spearman	U. S. Medical Corps.
Oscar O. Srp	Materials Laboratory Dept.USAF
Leonard Teitell	Frankford Arsenal, Philadelphia,Pa.
Gordon E. Terpenny	Power Plant Laboratory USAF
Elwood O. Titus	F.S.A., Bethesda, Md. Bethesda, Md.
William M. Upholt	U. S. Public Health Service
Harry S. Williams	Redstone Arsenal, Huntsville, Ala.
Arthur H. Wolff	U. S. Medical Corps
Joseph A. Zingales	U.S. Medical Corps

Twentieth Course

Marcelo Alonso	University of Havana
Ralph Adams	White Memorial Hosp., Los Angeles
William G. Anlyan	Duke University Hospital
John R. Cann	Univ. of Colorado Med. School
Julian H. Childs, Jr.	Jefferson Hosp., Philadelphia, Pa.
Leo V. Crowley	Medical College of Virginia,Richmond
Bernard J. DeWitt	Pittsburgh Plate Glass Co., Barberton, Ohio
Edgar E. Dickey	Institute of Paper Chemistry, Appleton, Wis.
A. Diez de Urdanivia	General Hospital of Mexico
W. M. Dugger, Jr.	University of Maryland
Richard B. Escue,Jr.	North Texas State College
Leland R. Felton	Mt. Zion Hospital, San Francisco
Stanley Green	Philadelphia General Hospital
James T. Grey	Cornell Aeronautical Lab.,Buffalo
Ralph E. Hartline	Stanolind Oil & Gas Co., Tulsa
Blair E. Hawkins	A.F. Res. Lab.,Cambridge, Mass.
Richard H. Hunt	Shell Oil Company, Houston
Wendell R. Koch	Materials Laboratory USAF
Seymour Levine	U. S. Public Health Service
Floyd E. Lovelace	Fish and Wildlife Service, Cortland, N. Y.
John P. O'Meara	Univ. of Oklahoma Medical Sch.
Richard A. Ormsbee	National Institute of Health, Hamilton, Mont.
Ovidio Laosa	Univ. of Havana Medical Sch.
Lester Lutes	U. S. Air Force
Hugh B. McManus	U. S. Air Force
Karl R. Paley	Lenox Hill Hospital, New York
Theodore R. Rice	Fish & Wildlife Service, Beaufort, N. C.
John J. Robinson	U.S.N.T.C. Great Lakes, Ill.
John B. Rowell	University of Minnesota
Jan Rydberg	University of Sweden, Stockholm
Asa Seeds	Memorial Hospital, Vancouver
Jack Shrader	U. S. Air Force
Mary T. Sullivan	Randolph Air Force Base
Vincent J. Seiwert	Cincinnati General Hospital
Wesley Whitehouse	U. S. Air Force
William A. Wolff	Bowman Gray School of Medic
Haruhisa Yoshikawa	Tokyo University Medical Coll

Twenty-First Course

Ferdinand Barnum	U. S. Air Force
Leslie F. Bates	University of Detroit
Richard H. Bohning	Ohio State University
Walter J. Burdette	LSU School of Medicine
Jameson L. Chassin	N. Y. University Medical School
Sam Frankel	Washington University Med. Sch.
James H. M. Henderson	Tuskegee Institute
Rowland E. Johnson	Florida State University
Ernest V. Jones	University of Alabama
Norman E. Kemp	University of Michigan
Martin D. Young	U. S. Public Health Service
S. C. Kirsch	Woodstock College
William H. Klein	Purdue University
Adrian C. Kuyper	Wayne Univ., Col. of Med.
William M. Layton, Jr.	Stamford (Conn.) Hospital
Sidney Larson	Aultman Hospital, Canton ,Ohio
Charles A. Leone	University of Kansas
Burley H. McCraw	VA Hospital, Houston, Texas
Donald W. Minteer	U. S. Army
Newman C. Nash	Wesley Hospital, Wichita, Kan.
Eddie Ortiz-Muniz	Agriculture & Mechanics Col. Mayaguez, Puerto Rico
Arthur Osol	Phila. College of Phar. & Sci.
Marion F. Magalotti	Cook County Hosp., Chicago
Joseph F. Migliorese	Rutgers University
Sava M. Roberts	VA Hosp., Augusta, Georgia
Joseph A. Rucker	A. & I. State College Nashville, Tenn.
William A. Scholes	Armour Res. Foundation, Chicago
Francis A. Spurrell	University of Minnesota
James M. Swain	U. S. Air Force
Alonzo Tenny	U. S. Air Force
Frederick K. Tsuji	Duquesne University
Clifford J. Webster	Evans Signal Lab., Belmar,N.J.

IV. Instrumentation Course.

N. Y. Anderson, Jr.	Cornell Aeronautical Lab.,Buffalo
F. E. Armstrong	U.S. Bureau of Mines, Bartlesville, Okla.
Dana W. Atchley, Jr.	Tracerlab, Inc., Boston
J. C. Atkinson	Wright-Patterson AFB
Glenn M. Burgwald	Nuclear Instrument & Chem.Corp., Chicago
Stanley H. Clark	General Elec.Co., Schenectady,N.Y.
William C. Cleveland	Radiation Counter Labs., Chicago
Louis Costrell	National Bureau of Standards,
Paul E. Damon	University of Arkansas
John M. Dorsey	University of Chicago
L. R. Everingham	Cornell Aeronautical Lab., Buffalo
Theodore Fields	Hines V-A. Hospital, Chicago

Gilson	University of Cincinnati
K. Halstead	Radio Corp. of America, Camden, N.J.
F. King	Wright-Patterson AFB
Kniazuk	Merck Inst. for Therapeutic Res.,
Kroosbein	Evansville (Ind.) College
M. Laing	Pittsburgh Plate Glass Co., Creighton, Pa.
W. Levine	Atlantic Refining Co., Philadelphia
rer	Naval Air Tech. Training Center, Memphis
McDonald	Sylvania Elec. Products, Inc., Bayside, N. Y.
L. Mell	Brown Instrument Co., Philadelphia
F. Merchant	Cincinnati Milling Machine Co.
Nader	U.S.P.H.S., Cincinnati
F. Oerlein	Army Chemical Center, Md.
A. Potter	Bell Telephone Labs., N. Y.
E. Romans	Univ. of Tennessee School of Med.
Shevick	University of Chicago
A. Smith	Wright-Patterson AFB
Townsend, Jr.	Army Chemical Center, Md.
J. Younker	University of Cincinnati
Wakefield	Radiation Counter Labs., Chicago

Advanced Course In Radioisotopes In Medicine

K. Alpert	George Washington University
Beierwaltes	University of Michigan Hospital
F. Bethard	University of Chicago
Briney	Hosp. of University of Pa.
Brown	Presbyterian Hospital, Chicago
Gould	Presbyterian Hospital, Chicago
W. Brown	Medical College of Georgia
A. Burrows	Cushing V.A. Hospital, Framingham, Mass.
Butler	Univ. of Nebraska College of Med.
Cameron	Hosp. of Woman's Medical College of Pa.

Walter H. Cargill	Emory University
Earle M. Chapman	Mass. Gen'l Hosp., Boston
Perk Lee Davis	Lankenau Hospital, Philadelphia
Henry H. Dunham	Univ. Hospitals, State University of Iowa
H. B. Elkins	Univ. Hospitals, State University of Iowa
Lowell A. Erf	Jefferson Hosp., Philadelphia
Archie Fine	Jewish Hosp., Cincinnati
S. Taplits	Jewish Hosp., Cincinnati
Jacob R. Freid	Montefiore Hosp., N. Y.
Harry J. Greene	Kings County Hosp., Brooklyn, N.Y.
W. L. Hawley	Los Alamos Medical Center
Irvin F. Hummon	Cook County Hopsital, Chicago
Tyra T. Hutchens	Univ. of Oregon Medical School
Richard H. Kirkland	Medical College of Va.
Ross C. Kory	VA Hospital, Nashville
Frederick C. Kittle	Univ. of Kansas Medical Center
Arthur L. Kretchmar	University of Michigan
Samuel Leo	Fordham University Hospital
J. W. Lewis	Colorado Springs Medical Center
George B. McAdams	Hartford (Conn.) Hospital
Jack G. S. Maxfield	Maxfield X-ray & Radium Clinic, Dallas
Leo M. Meyer	Goldwater Memorial Hosp., N. Y.
Paul J. Murison	Tulane University
Y. T. Oester	Stritch School of Med., Chicago
O. S. Peterson, Jr.	Univ. of Vermont Sch. of Med.
Donald W. Petit	Univ. of Southern Calif. Med. Sch.
Robert Robbins	Temple Univ. Hosp., Philadelphia
Lindon Seed	Grant Hospital, Chicago
David Shapiro	Univ. of Louisville Sch. of Med.
Samuel E. Sinberg	Hosp. for Joint Diseases, N. Y.
Julius D. Taylor	Abbott Labs., Chicago
William V. Tenzel	Beth Israel Hosp., N. Y.
George E. Thoma	St. Louis Univ. School of Med.
George Z. Williams	Medical College of Virginia

APPENDIX V

MUSEUM DIVISION

ical Advisory Committee

C. Aebersold	Atomic Energy Commission
A. Andrews	OR Inst. of Nuclear Studies
Comar	UT-AEC Ag. Res. Program
A. Conners	K-25
D. Cowen	ORNL
B. Emlet	Oak Ridge National Lab.
F. Hemphill	Y-12
F. Kimbell	Oak Ridge National Lab.
Macklin	K-25
McCrady	Atomic Energy Commission
J. Murphy	Oak Ridge National Lab.
Rydzewikis	Atomic Energy Commission
D. Susano	Y-12
Western	Oak Ridge National Lab
A. Wiggin	Atomic Energy Commission

II. Organized Groups Visiting Museum

Allardt Elem. Sch.	Allardt, Tenn.	45
American War Mothers	Akron, Ohio	30
Antioch College	Yellow Springs, Ohio	15
Athens Bible Sch.	Athens, Ala.	18
Baxter Seminary	Baxter, Tenn.	65
Bearden High Sch.	Bearden, Tenn.	23
Bethesda High Sch.	Thompson Stat., Tenn.	18
Bentonville High Sch.	Bentonville, Ind.	19
Bluefield State College	Bluefield, W. Va.	14
Boy Scout Troup No. 185	Columbia, Ky.	22
Bryan University	Dayton, Tenn.	29
Bungalow Elem. Sch.	Maryville, Tenn.	38
Campbellsville College	Campbellsville, Ky.	41
Campfire Girls	Oak Ridge, Tenn.	10

Carson Newman College	Jefferson City, Tenn.	24
Center Township High	Osgood, Ind.	29
Central High Sch.	Columbia, Tenn.	34
Chattanooga Girl Scouts	Chattanooga, Tenn.	24
Chattanooga High Sch.	Chattanooga, Tenn.	12
Chattanooga Valley High	Chattanooga, Tenn.	38
Chilhowee View Sch.	Maryville, Tenn.	35
Clemson College	Clemson, S. C.	14
Clinton High Sch.	Clinton, Tenn.	31
Coal City High Sch.	Coal City, Ind.	13
Concord Township High	St. Joe, Ind.	18
Crichloui Jr. High Sch.	Murfreesboro, Tenn.	44
Cub Scouts, Troup 3225	Oak Ridge, Tenn.	12
Cub Scout, Troup 31	Knoxville, Tenn.	8
Cumberland Co. Schs.	Cumberland Co., Tenn.	8
David Millard Jr. High	Asheville, N. C.	117
Dobyns Bennett High	Kingsport, Tenn.	46
Edmund Embury Sch.	Tryon, N. C.	29
East Tenn. Auto. Club		57
State Teachers College	Johnson City, Tenn.	46
Eaton Elem. Sch.	Lenior City, Tenn.	31
Etowah High Sch.	Etowah, Tenn.	32
Everett High Sch.	Maryville, Tenn.	33
Farragut High Sch.	Concord, Tenn.	38
First Pres. Church	Sunset Gap, Tenn.	22
Franklin High Sch.	Franklin, N. C.	54
Gatlinburg High Sch.	Gatlinburg, Tenn.	18
Girl Scout Troup No.30	Oak Ridge, Tenn.	15
German Orientation Prog.	Duke University	11
Girls Preparatory Sch.	Chattanooga, Tenn.	31
Hall Fletcher Jr. High	Asheville, N. C.	78
Hillandale Sch.	Ft. Lauderdale, Fla.	6
Hi Valley Camp		30
Hiwassee College	Madisonville, Tenn.	12
Home Demonstrators	State of Tenn.	26
Jefferson Jr. High Sch.	Oak Ridge, Tenn.	163
Jonesville High Sch.	Jonesville, Va.	24
King College	Bristol, Tenn.	18
Kingwood Sch.	Tate Spring, Tenn.	47
Kirkwood Community	Clarksville, Tenn.	13
Knox. Evening High	Knoxville, Tenn.	35
Knox. Journal Carriers	Knoxville, Tenn.	97
Lanier High Sch.	Maryville, Tenn.	44
Lee College	Cleveland, Tenn.	40
Lincoln Memorial Univ.	Harrogate, Tenn.	32
Little Creek High Sch.	Concord, Tenn.	25
Livingston High Sch.	Livingston, Ky.	11
Lower Windrock Sch.	Oliver Springs, Tenn.	16
Mary Hughes High Sch.	Piney Flats, Tenn.	22
McMinn County High	Athens, Tenn.	41
Methodist Ministers		31
Methodist Youth Fellowship		50
Middleburg High Sch.	Middleburg, Ky.	22
Midway High Sch.	Kingston, Tenn.	12

M. I. T. Class A-51	Cambridge, Mass.	[illegible]
M. I. T. Practice Sch.	Cambridge, Mass.	[illegible]
Monterey High Sch.	Monterey, Tenn.	[illegible]
Moorhead High Sch.	Moorhead, Miss.	[illegible]
Morristown High Sch.	Morristown, Tenn.	[illegible]
Pres. SE Seminar		[illegible]
Nat'l Ass'ns of Power Engrs.		[illegible]
Navy Radiation Sch.		[illegible]
New Market High Sch.	New Market, Tenn.	[illegible]
Ohio State University	Columbus, Ohio	[illegible]
Piedmont High Sch.	Piedmont, Ala.	[illegible]
Peavine Baptist Church	Rock Springs, Ga.	[illegible]
Park City High Sch.	Park City, Ky.	[illegible]
Pleasant Hill High Sch.	Crossville, Tenn.	[illegible]
Piqua High Sch.	Piqua, Ohio	[illegible]
Rhea Central High Sch.	Dayton, Tenn.	[illegible]
Red Bank High Sch.	Chattanooga, Tenn.	[illegible]
Roane County High	Kingston, Tenn.	[illegible]
Robbins Elem. Sch.	Robbins, Tenn.	[illegible]
Robbins High Sch.	Robbins, Tenn.	[illegible]
Robert Huff Sch.	Knoxville, Tenn.	[illegible]
Rockford Elem. Sch.	Rockford, Tenn.	[illegible]
Rogersville High Sch.	Rogersville, Tenn.	[illegible]
Rotary Club Members		[illegible]
Sampson Elem. Sch.	Pikeville, Tenn.	[illegible]
Science Hill High Sch.	Johnson City, Tenn.	[illegible]
Sigma Phi Sigma Conven.		[illegible]
Smithwood Sch.	Knoxville, Tenn.	[illegible]
South Clinton Sch.	Clinton, Tenn.	35
St. James High Sch.	Greene County, Tenn.	[illegible]
Stockbridge High Sch.	Interlaken, Mass.	14
So. Bell Tel. Employees		[illegible]
Sweetwater High Sch.	Sweetwater, Tenn.	11
Tenn. Hardware Ass'n		50
Farmer-Rancher Tour	State of Texas	121
Tennessee High Sch.	Bristol, Tenn.	55
Trevecca High Sch.	Nashville, Tenn.	20
Turkish Delegates &T.V.A.		5
Univ. of Alabama	Tuscaloosa, Ala.	19
Univ. of Chattanooga	Chattanooga, Tenn.	25
Univ. of Tennessee	Knoxville, Tenn.	52
Vanderbilt Univ.	Nashville, Tenn.	16
Virginia Intermont Col.	Bristol, Va.	7
Western Reserve Acad.	Hudson, Ohio	16
Washington Local High	Ney, Ohio	10
Webb High Sch.	Bell Buckle, Tenn.	11
Wheeler Co. High Schs.	Weeler County, Ga.	60
Whitwell High Sch.	Whitwell, Tenn.	14
State Teachers College	Willimantic, Conn.	22
Young High Sch.	Knoxville, Tenn.	21
Youth, Incorporated	Nashville, Tenn.	25
	TOTAL VISITORS	3,989
	TOTAL GROUPS	119

6/30/52

Sixth Annual Report

of the

Oak Ridge Institute of Nuclear Studies

June 30, 1952

Operating Under Contract

With the

UNITED STATES ATOMIC ENERGY COMMISSION

AEC, Oak Ridge, Tenn. 10-6-52-3,000-W-20430

Medical Division

THE major development in radiation therapy during the year was the emergence of teletherapy units and the prospect that they would become widely available in a few years. The Medical Division established itself at the forefront of this development in keeping with its role of taking on those problems for which it is especially well equipped to handle by virtue of location, staff or equipment. Highlights of the year were the delivery in October of the Cobalt^{60} teletherapy unit and the initiation of plans through the Institute Council for a major teletherapy evaluation program in cooperation with the Southern Medical Schools.

This does not mean a decreased effort in the study of internally-administered isotopes. On the contrary, every radiation treatment given during the year was by internally-administered radioisotopes or by standard x-ray treatment. Moreover, the continued improvement of radiogold therapy in the Medical Division and elsewhere is one of the brighter features of cancer research at this time. Gallium^{72} was abandoned during the year as a possible treatment; on the other hand, treatment was begun with Gallium^{67} to see if this isotope fulfilled some of the hope formerly held for Gallium^{72}. Research continued on hafnium and a number of other isotopes which may be tested therapeutically.

TELETHERAPY EVALUATION PROJECT

At the AAAS Symposium on cancer research in Philadelphia last December, Dr. Max Cutler, director of the Chicago Tumor Institute, predicted that the approaching development of teletherapy units, using products from the atomic energy program, would revitalize the entire field of radiology. The teletherapy evaluation program now in process of development by the Institute and associated medical schools lends credence to Dr. Cutler's prediction. For the fact remains that with the exception of hormonal treatment of certain types of cancer, radiation and surgery continue to be the most successful treatment available. Again paraphrasing Dr. Cutler, a slight improvement in present treatment techniques often means the difference in saving or losing a patient. Teletherapy units offer quite important possibilities for improved cancer treatment.

The question of a full-scale development program was first brought up in discussions of the Medical Advisory Panel. Later, the Medical Committee of the Council studied the proposal and gave it strong support as an excellent example of the type cooperation which should be carried out between the Institute and its sponsoring universities and the regional medical schools. The Council committee urged the Board of Directors of the Institute to support such a plan, which the Board did at its March 31 meeting. On May 15-16 a two-day meeting of medical school representatives was held at Oak Ridge to explore the proposal at some length. This group voted unanimously to recommend that the project be undertaken through a plan whereby the Medical Division would build a teletherapy unit. From this prototype, a Teletherapy Evaluation Board from cooperating medical schools will attempt to delineate the specifications for a standard model. Following adequate testing, similar units would be procured by certain of the medical schools for a more thorough clinical testing program.

The group left open the decision as to whether cesium, cobalt or europium would be the radiation source. Each has its enthusiasts. Cesium is a fission product of high yield. (More than 6% of uranium fission products is cesium.) It has a .667 mev gamma ray and a 33-year half-life. Cobalt has a 1.2 mev gamma ray and a 5.3-year half-life. It is produced by neutron irradiation and is available in high intensity sources. Europium has a wide spectrum of gamma ray energies and a 5.35 year half-life and is also a neutron-induced radioisotope. Much interest has been shown in europium because of the high intensity theoretically possible with short-term irradiation--550 curies per gram of material compared with 20 curies per gram of cobalt (irradiated in a reactor with a neutron flux of $7 \times 10^{12}/cm^2/sec$) and 20 curies per gram of cesium. Radium is roughly one curie per gram. A europium source could be 100 times smaller than a comparable cobalt teletherapy source.

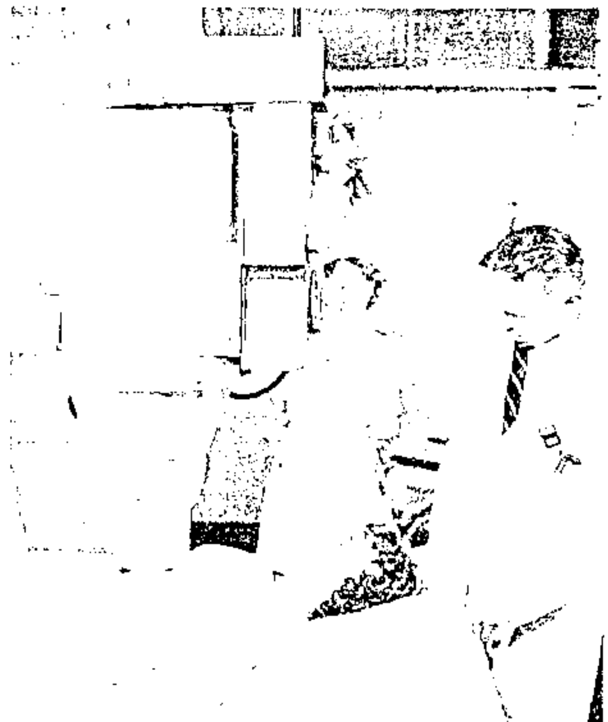
The use of any of the three sources presents difficulties. The separation of cesium from other fission products is now on a "test tube" scale. While these operations will result in a few sources of several kilocuries becoming available in the next few years, production of any appreciable number will not be possible until after 1956.

Both cobalt and europium are dependent on much reactor time becoming available. In an address before the American Radium Society meeting in Chicago on June 10, 1952, Paul C. Aebersold, Director of the AEC Isotopes Division, said that a good supply of high specific activity Cobalt^{60} would become available by 1954 from high flux reactors now being put into operation in this country. The principal limitation in the use of Europium^{152,154} as a teletherapy source is the unavailability of a sufficient supply of the rare earth element for target material. Moreover, the europium target material would need to be very pure since some of the rare earth elements from which it would have to be extracted have even higher neutron capture cross-sections than europium.

W. W. Grigorieff, Director of the Institute of Science and Technology of the University of Arkansas and Chairman of the Council Medical Committee, reported on the project at the annual meeting in June and urged its support by the Council as a whole. His report was unanimously supported by the Council. This was the status at year's end.

COBALT^{60}

The development of a cobalt^{60} teletherapy unit has been a joint project of the University of Texas M. D. Anderson Hospital for Cancer Research and the Institute since July, 1950. The unit was completed and placed in operation at the Institute this year, although a low priority in the Chalk River (Canada) reactor has delayed delivery of the 800-curie source. In the meantime the Medical Division arranged to borrow from Oak Ridge National Laboratory a 200-curie source belonging to Dr. Max Cutler of the Chicago Tumor Institute to carry out tests of the unit. The teletherapy unit was built by the X-Ray Department of the General Electric Company to specifications worked out jointly by M. D. Anderson and Institute personnel. The project is jointly directed by H.D. Kerman, M. D., radiologist with the Medical Division, and Gilbert N. Fletcher, M. D., radiologist with M. D. Anderson Hospital. The unit is being tested at Oak Ridge by Dr. Kerman and Jasper E. Richardson, Ph.D., a research participant from M. D. Anderson Hospital.



COBALT TELETHERAPY UNIT

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GALLIUM

The Medical Division abandoned Gallium^{72} during the year as a treatment isotope for bone tumors, either primary or metastatic. A pile-produced isotope, Gallium^{72} could not be obtained except in small quantities carried in much larger amounts of stable Gallium$^{69-71}$. Since the metal is toxic, it was not possible to give sufficient radiation doses. A comprehensive report of the gallium project has been made to the Sub-Committee on Human Use of the Committee on Bioloby and Medicine of the AEC and will be published as a supplement to *Radiology* in a future issue.

The Division next turned to Gallium^{67} to determine whether this isotope would do what Gallium^{72} failed to do: deliver a heavy radiation dose to the tumor with a tolerable metal and radiation dose to the organism as a whole. In the first place, it was available in highest purity from the bombardment of zinc in the Oak Ridge cyclotron and was easily separated from the parent element, zinc. Its half-life of 3¼ days is far more desirable than the 14.2-hour half-life of Gallium^{72} (much of the activity of Gallium^{72} was dissipated by the time it had reached the tumor), and its low gamma energies are more desirable than the very high energies of Gallium^{72}.

Preliminary tests of Gallium^{67} by Dr. H. D. Bruner revealed an interesting phenomenon: In pure form, its distribution was quite unlike that of carrier-borne Gallium^{72}. By mixing a small amount of stable carrier gallium with the radioisotope, Gallium^{67} distribution matched that of the other isotope.

While the dose to the liver, a radio-sensitive organ, seems discouragingly high, it must be remembered that it is impossible to give radiation treatment of any kind without some destruction of normal body tissues. Furthermore, animal tests indicate that the liver may reach a saturation point and that a heavier dose may increase the concentration in tumor in relation to the liver dose.

In passing, the Division acknowledges a great debt to the Oak Ridge National Laboratory in the Gallium^{67} work. There is intense competition for time in the Oak Ridge cyclotron, but the Division is able to get sufficient amounts of Gallium^{67} for its work. The Analytical Chemistry Division of the Laboratory computed the decay scheme of Gallium^{67}, a difficult job requiring exceptional equipment and know-how. The work of Raymond L. Hayes, of the Medical Division staff, on the chemistry of gallium and its preparation for human use also was noteworthy.

GOLD PROGRAM

During the past year the Medical Division has continued its program of study of the therapeutic value of colloidal radiogold. The chief ca phasis has been on the intracavitary use of this isotope. The clinical results of this form of treatment for palliation of advanced neoplasms is being studied at several medical centers. It was felt that the chief contribution that the Medical Division might make would be a very careful investigation of the fate and distribution of the isotope when it is used in this manner; consequently, many assays have been done of activity levels and tissue and ascitic fluid, as well as blood radioactivity levels and tissue assays. These studies have led to the conclusion that a small to moderate amount of the gold leaves the cavity into which it is injected and travels to the reticuloendothelial tissues of the body; thus, there is some radiation of these sensitive tissues from locally deposited gold, as well as from the gamma emission of the large volume of isotope in the cavity itself. Hematologic studies indicate that there are definite radiation changes in the blood and bone marrow after doses used for therapy, but these changes do not seem to be of great significance in patients with a relatively poor prognosis. They would lead to some hesitancy in giving large doses of this isotope to patients without known metastatic tumor.

The Medical Division has also been interested in the intravenous use of this isotope, and a few patients with metastatic or primary tumors of the liver have been given intravenous injections of the radiogold. It has appeared quite clear that this is an ineffectual form of treatment, because of the large size of the tumor nodules and the failure of the gold or its rays to penetrate these lesions, even though the surrounding liver parenchyma may contain a large amount of radioactive gold.

Because the beta rays from $Gold^{198}$ have so little penetrating power, there has been considerable interest in using an isotope with a more penetrating form of radiation. As an example, colloidal chromic phosphate containing P^{32} is under consideration. This has already been used on the West Coast, but there is very little basic data on its distribution, degree of ionization and so forth. The Division is now launching a program along with several other groups in the country to study a chromic phosphate preparation which may be used for intracavitary and intravenous injection.

STAFF

The Division is suffering a severe loss in the resignation of two of its senior staff members, effective July 1, 1952. Dr. H. D. Bruner, Chief Scientist of the Division, is now at the Emory University Medical School as Professor and Chairman of the Department of Physiology. Jesse D. Perkinson, Ph. D., Senior Scientist in the Division, has joined the University of Tennessee College of Medicine as Associate Professor of Biochemistry. Dr. Bruner was the first scientist employed by the Division following its organization, and Dr. Perkinson came only a short time later.

The Division also lost several of its technical and administrative personnel. A number left to continue their education, while others accepted different jobs for salary or other personal reasons.

On the positive side, two staff additions during the year have added strength to the program. Dr. Betty M. Cooper, Anesthesiologist to the Oak Ridge Hospital and Senior Scientist in the Medical Division, has been a valuable addition to the staff. Dr. Ralph Kniseley, Pathologist to the Oak Ridge Hospital and Principal Scientist in the Medical Division, has added greatly to the effectiveness of the Division in developing and supervising the heavy load of work in pathology, including autoradiography, which the clinical research program involves.

CARE AND TREATMENT OF PATIENTS

The Division accepted 189 patients for treatment during the year. In spite of the limited budget on which the Division operates, every effort is made to keep the patients comfortable and occupied. An outdoor terrace was built during the year. (It was landscaped by the Medical Division Staff, and patient rooms were air-conditioned.) Mrs. Priscilla A. Oliver, physical therapist, has established an extensive program to occupy the patient's time in worthwhile ways. (One patient made considerable pocket money by turning out hand-tooled leather billfolds.) The Division is particularly fortunate in having Dr. Gould Andrews serving it in the capacity of Chief of Clinical Services. His sympathetic understanding and concern for the patients, as well as his exceptional clinical knowledge and ability have imbued the entire clinical and nursing staff with a sense of mission which has contributed much to the program.

TRAINING PROGRAM

There were nine resident physicians from the medical schools, one of whom was Dr. Chiyeko Okawa from Tokyo, Japan, who came to the Medical Division as resident physician through the University of Alabama Medical School. During the year there were eight Air Force resident physicians assigned to the Medical Division for approximately 90 days each. There were three other resident physicians from other branches of the U.S. Armed Forces. During the year the following scientific personnel visited and worked in the Medical Division: John R. Horan, an employee of the Phillips Petroleum Corporation and former Radiological Physics fellow, spent six months working with George A. Boyd and other members of the senior staff. Giovanna Mayr, Ph.D., of the University of

Milan, spent five months working with Dr. Bruner and other members of the senior staff. Liselotte Schachinger and Hilde Fiedler spent approximately five months working with Dr. Perkinson. These German scientists were studying at the University of Tennessee under the Fulbright program. Dr. Enrico Via, radiologist from the Rome, Italy, Cancer Institute, was an investigator with the Division for three months.

ASSISTANCE FROM OAK RIDGE PHYSICIANS

For over two years the Medical Division of the Institute has been fortunate in being able to call upon physicians with specialized training who are in practice in Oak Ridge, to supplement the help given by consultants from the medical schools. Because of the relatively small staff of the Medical Division, the various medical specialties cannot be represented on the permanent staff, and without this larger consulting staff, it would be difficult to provide complete medical care for the patients or to carry out all of the research activities.

Several phases of the Medical Division program involve surgical treatment. Tissue specimens are often obtained in order to determine isotope distribution and to decide upon the advisability of further treatment with isotopes. Patients with thyroid carcinoma, bone tumors, and fluid-producing tumors in the abdomen may require surgery while in Oak Ridge, even though many of them have had extensive surgical treatment before being sent here. In particular, the staff is grateful for the help of three Oak Ridge surgeons, Dr. Robert Bigelow, Dr. Dana Nance and Dr. Paul Spray, who have performed many operations upon patients in the Medical Division Hospital. Various types of consultant services have been needed, and several other physicians from Oak Ridge and Knoxville have contributed assistance in particular phases of the work.

The full-time staff is genuinely appreciative of the importance of this contribution and is heartened by this evidence of interest and approval of the program of the Division.

APPENDIX I

PERSONNEL OF THE OAK RIDGE INSTITUTE OF NUCLEAR STUDIES

(as of July 1, 1952)

A. Council

David H. Morgan	A & M College of Texas
Fred Allison	Ala. Polytechnic Institute
Karl F. Herzfeld	Catholic Univ. of America
H. L. Hunter	Clemson Agricultural College
W. M. Nielsen	Duke University
J. Gordon Stipe	Emory University
M. W. Carothers	Florida State University
R. L. Sweigert	Georgia Institute of Technology
R. C. Keen	Louisiana State University
M. P. Etheredge	Mississippi State College
C. K. Beck	North Carolina State College
T. W. Bonner	Rice Institute
R. T. Nieset	Tulane University of Louisiana
Marten ten Hoor	University of Alabama
W. W. Grigorieff	University of Arkansas
R. B. Eutsler	University of Florida
G. H. Boyd	University of Georgia
Lyle Dawson	University of Kentucky
R. C. Ernst	University of Louisville
Ronald Bamford	University of Maryland
P. K. McCarter	University of Mississippi
C. D. Van Cleave	University of North Carolina
Simon H. Wender	University of Oklahoma
Facundo Bueso	University of Puerto Rico
Harry W. Davis	University of South Carolina
E. A. Waters	University of Tennessee
C. P. Boner	University of Texas
John H. Yoe	University of Virginia
M. D. Peterson	Vanderbilt University
Louis A. Pardue	Virginia Polytechnic Institute

B. Board of Directors

Paul Magnus Gross, *President*
Vice President, Duke University

Jesse Wakefield Beams, *Vice President*
Professor of Physics, University of Virginia

George H. Boyd, *Director & Chairman of the Council*
Dean of the Graduate School, University of Georgia

John Ray Dunning, *Director*
Dean of Engineering, Columbia Uni[illegible]

William Vermillion Houston, *Director*
President, Rice Institute

Samuel Colville Lind, *Director*
Technical Advisor, Carbide & Car[illegible]
Chemicals Company, Oak Ridge

Hayden C. Nicholson, *Director*
Dean, School of Medicine, University of Arkansas

Theophilus Shickel Painter, *Director*
President, University of Texas

Louis Arthur Pardue, *Director*
Vice President, Virginia Polytechnic Institute

[illegible] Personnel

OFFICE OF THE EXECUTIVE DIRECTOR

William G. Pollard, Executive Director

George B. Pegram, Consultant

[illegible] Joy Clapp	Record Clerk
[illegible] R. Davis	Sr. Record Clerk
[illegible] Ethridge	Record Clerk
[illegible] H. Garber	Librarian
[illegible] H. Gimera	Secretary
[illegible] Halburnt	Clerk-typist
[illegible] Izon	Record Clerk
[illegible] Johnson	Head, Information Dept.
[illegible] Lent	Sr. Record Clerk
[illegible] Lewis	Sr. Secretary
[illegible] Markel	Librarian
[illegible] Mumford	Assistant Treasurer
[illegible] Rutherford	Auditor
[illegible] Schlueter	Library Supervisor

OFFICE OF ADMINISTRATION

Paul M. Elza, Manager of Administration

[illegible] F. Benton	Accountant
[illegible] L. Blankenship	Maintenance Mech. I
Fern C. Brewster	Clerk-typist
Ralph B. Briggs	Maintenance Mech. II
John Burns	Mail Clerk (temp.)
Joan R. Clouse	Receptionist
Barbara Cole	Stenographer
Paul G. Davis	Storekeeper
Charles H. Day	Stockkeeper
B. J. DeLozier	Secretary
Stanley Denny	Helper (temp.)
W. Gilbert Disney	Accounting Clerk
William Dumas	Helper
Harrison E. Elliott	Purchasing Agent
Ellen Epperson	Accountant
John H. Fenton	Head, Manag. Services Dept.
Dewey Ferguson	Maintenance Mech. I
Walter E. Graves	Maintenance Mech. I
Barbara R. Guinn	Clerk-typist
Johnnie Harvest	Helper (temp.)
Nathaniel W. Hill	Instrument Engineer
Beatrice M. Holtzclaw	Clerk-typist
Joseph C. Houston	Photographer
Billie J. Hurt	Clerk-typist (temp.)
Dorothy L. Johnson	Stenographer
Faye J. Jones	Clerk-typist

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Harry E. Kimble	Instrument Maker
Arch E. Long	Maintenance Mech. I
Barbara McClannahan	Admin. Services Supervisor
T. W. Martin	Head, Tech. Services Dept.
Dorothy Nanney	Accounting Clerk
William R. Perry	Mail Clerk
B. J. Pitts	Helper (temp.)
William Rhodey	Maintenance Mech. II
J. W. Rose	Head, Fiscal Services Dept.
Jenny Rose	Clerk-typist (leave of absence)
Gloria Roseberry	Vari-typist
H. J. Russell	Maintenance Mech. I. (temp.)
Mary E. Russell	Office Services Supervisor
Wendell Russell	Administrative Assistant
W. D. Schwartzman	Property & Supply Asst.
*William L. Scott	Mech. Engineer
Hugh Simpson	Custodian
Robert Taylor	Custodian
Rosella Tindell	Clerk-typist
Henry Thomas	Maintenance Mech. II
Marvin Triplett	Maintenance Mech. II
Nancy Vail	Record Clerk
Charles L. Vaughn	Chief Maintenance Mech.
Johnny Vaughn	Delivery Man
L. Vickery	Helper (temp.)
*Donald D. Walker	Instrument Maker
Charles Wallace	Cabinet Maker
Marjorie Whittlesey	Stenographer
James Wilde	Instrument Maker

UNIVERSITY RELATIONS DIVISION

Russell S. Poor, Chairman (on leave of absence)

Marion T. Clark, Acting Chairman

Vera E. Coffey	Stenographer
Donna Dinsmore	Record Clerk
William Dryden	Administrative Asst.
Trula Hobbs	Secretary
Lesta Prater	Clerk-typist
Nelle Strange	Administrative Aide

MEDICAL DIVISION

Marshall Brucer, Chairman

Gould A. Andrews	Chief, Clin. Services
Mary C. Bondurant	Laboratory Tech.
George A. Boyd	Sr. Scientist
William R. Buher	Research Asst.
Elmer A. Carpenter	Custodian
Mabel L. Carroll	Stenographer
Betty M. Cooper	Sr. Scientist
Betty R. Cooper	Laboratory Tech.
Henry P. Copeland	Laboratory Tech.
Edgar A. Cress	Research Tech.
Rachel C. Dixon	Laboratory Aide
Lewis Dobson	Helper
Timothy Dowdell	Helper
Nelda Edwards	Med. Records Librarian
James E. Eldridge	Research Assoc.
William C. Fields	Laboratory Asst.
Eula B. Francis	Stenographer
William D. Gibbs	Laboratory Tech.
Robert J. Gibson	Laboratory Tech.
J. Howard Harmon	Administrative Officer
Raymond L. Hayes	Scientist
Eva Hodgens	Laboratory Tech.
Elmer L. Keller	Laboratory Tech.
Herbert D. Kerman	Prin. Scientist
Ralph M. Kniseley	Prin. Scientist
Granvil S. Kyker	Prin. Scientist
Vivian D. Lay	Clerk-typist (temp.)
Dorothy M. Lewis	Stenographer
Wallace K. Luke	Laboratory Tech.
William C. Martin	Laboratory Asst.
Francis G. McMahon	Lab. Tech. (temp.)
*Priscilla A. Oliver	Occup. Therapist
Dorothy Osteen	Secretary
Blanche Richardson	Receptionist
Mary E. Roberts	Clerk-typist (temp.)
Samuel Root	Clinician
Edward M. Russ	Laboratory Tech.

SPECIAL TRAINING DIVISION

Ralph T. Overman, Chairman

Joseph E. Eve	Lab. Aide
Ralph H. Firminhac	Scientist
Iziah Jones	Custodian
Elizabeth Rona	Sr. Scientist
Charles S. Simons	Sr. Scientist
Frances E. Smellage	Secretary
Donald R. Smith	Scientist
Ardell Craig Stewart	Lab. Assistant
Edith Wilson	Secretary

EXHIBITS DIVISION

David L. DeJarnette, Chairman

Margaret K. Brooks	Secretary
Charles S. Davis	Museum Aide (temp.)
W. Earl Duff	Exhibits Manager
Jean E. Fahey	Receptionist
Wheeler Fain	Custodian
John N. Fox	Museum Aide
Renfro Henderson	Custodian
Jack D. Johnson	Museum Aide
Alice N. Montgomery	Clerk-typist
Robert R. McDonald	Maintenance Mech. I
Harold E. Price	Display Artist
Theodore J. Robbins	Maintenance Mech. I
Donald G. Robertson	Museum Assistant
Robert C. Rothermel	Museum Aide
L. H. Sharp	Preparator

TERMINATIONS

OFFICE OF THE EXECUTIVE DIRECTOR

Dorothy Matthews	Sr. Secretary

OFFICE OF ADMINISTRATION

Mary C. Argo	Stenographer
Dorothy B. Brown	Administrative Aide

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Josephine C. Butler	Stenographer
Walter Clevenger	Mail Clerk
F. W. Eades	Prop. & Supply Asst.
Ann R. Estep	Receptionist
William D. Helwig	Instrument Maker
Dorothy M. Holloway	Clerk-typist
Jay G. Howell	Janitor
Ida C. Johnson	Stenographer
Lena R. Jones	Secretary
Mary Adele Keyes	Stenographer
Claude McCallum	Bookkeeper
Claude E. McGill	Accountant
Gladys M. Mercer	Stenographer
John A. Mott	Bookkeeper
Clyde Parton	Helper
Ruth M. Reed	Budg. & Proced. Asst.
William C. Rose	Warehouse Supervisor
Florence N. Stanford	Stenographer
Betty Jean Thomas	Receptionist
Charles L. Vaughn	Chief Maint. Mech.
Willie G. Waller	Helper (temp.)
H. M. Whittlesey	Maintenance Mech. I
Albert Williams	Helper

UNIVERSITY RELATIONS DIVISION

Mary S. Kinsey	Stenographer
Juanita H. Looney	Stenographer
Barbara A. Miller	Clerk-typist
Lois M. Rowe	Secretary
Marjorie A. Smith	Clerk-typist

MEDICAL DIVISION

Harry D. Bruner	Chief Scientist
John P. Byrom	Health Physicist
Joe R. Cantrell	Laboratory Tech.
Blanche Carden	Stenographer
Walter H. Cargill	Research Asst.
Bonnie L. Cook	Receptionist
Hugh M. Dobson	Orderly
John Gallimore, Jr.	Research Asst.
Mary Stebbins Gude	Laboratory Tech.
Anna R. Henley	Custodian
Maryann Heppert	Laboratory Tech.
Grey B. Kornegay	Resid. in Exp. Med.
Jesse D. Perkinson	Sr. Scientist
Helen S. Randolph	Laboratory Tech.
Robert Sellers	Research Tech.
William Smith	Laboratory Tech.
Mary P. Smyser	Laboratory Tech.
Frieda R. Urey	Laboratory Tech.
Alice H. Whitson	Med. Records Libr.
G. Curtis Wilson	Research Tech.

SPECIAL TRAINING DIVISION

Herbert M. Clark	Instructor
Walter Clossey	Audio-Visual Tech.
Rex G. Fluharty	Sr. Scientist

EXHIBITS DIVISION

Margaret M. Abdian	Secretary
Carolyn M. Bradford	Museum Aide
Lennie A. Childress	Stenographer
Basil E. Martin	Curator
Andrew C. Smith	Museum Aide

III. Consultant

George B. Pegram

APPENDIX II

UNIVERSITY RELATIONS DIVISION

I. Research Participants Beginning Appointments During Fiscal Year 1951-52

Institutions, participants, and laboratories, where research was carried out.

Sponsoring Universities

A & M College of Texas	
Royce H. LeRoy	ORNL
George M. Watson	ORNL
Alabama Polytechnic Institute	
Robert F. Clothier	ORNL
Thomas F. Goldcamp	ORNL
Ernest Ikenberry	ORNL
Justin T. Long	ORNL
Duke University	
Karl M. Wilbur	ORNL
Emory University	
Ernest L. Hunt	ORNL
William H. Jones	ORNL
Florida State University	
Rowland E. Johnson	ORNL
George L. Rogosa	ORNL
Raymond K. Sheline	ORNL
Georgia Institute of Technology	
Royal F. Sessions	ORNL
Allan C. Topp	ORNL
Louisiana State University	
Max Goodrich	ORNL
Richard C. Keen	ORNL
Maurice M. Vick	ORNL
Mississippi State College	
Arnold J. Gully	ORNL
North Carolina State College	
Ernest A. Ball	ORNL
Elma Lanterman	ORNL
Joseph T. Lynn	UT-AEC
Rice Institute	
Jurg H. E. Waser	ORNL
Tulane University of Louisiana	
Walter S. Wilde	ORNL

Max Planck Institut
Goettingen, Germany

Ferrell, Richard A.	W. Heisenberg	Calif. Inst. of Technology	Physics

University of Copenhagen
Copenhagen, Denmark

Mottelson, Ben R.	Niels Bohr	Purdue Univ.	Physics

APPENDIX III

MEDICAL DIVISION

Medical Advisory Panel

George T. Harrell, Chairman
Bowman Gray School of Medicine

R. Lee Clark	M. D. Anderson Hospital
Wilburt C. Davison	Duke University
Manuel Garcia	Tulane University of La.
Hayden C. Nicholson	University of Arkansas
Vernon W. Lippard	University of Virginia
Paul W. Schafer	University of Kansas
Douglas H. Sprunt	University of Tennessee

Consultants to Medical Division

Paul C. Aebersold	Atomic Energy Commission
Jerry K. Aikawa	Bowman Gray School of Medicine
Charles R. Allen	University of Texas Medical Branch
John Robert Andrews	Bowman Gray School of Medicine
Ludwick Anigstein	Univ. of Texas Medical Branch
W. R. Arrowsmith	Ochsner Clinic, New Orleans
Camillo Artom	Bowman Gray School of Medicine
Carl T. Bahner	Carson Newman College
[illegible] Bauer	Univ. of Michigan School of Med.
Joseph W. Beard	Duke Univ. School of Medicine
Harold F. Berg	Univ. of Louisville School of Med.
Robert R. Bigelow	Oak Ridge Hospital
Harvey Blank	Univ. of Penn. School of Med.
Walter L. Bloom	Emory Univ. School of Medicine
Ralph R. Braund	Univ. of Tennessee Sch. of Med.
Robert L. Brown	Emory University Hospital
Stephen W. Brown	Georgia School of Medicine
Walter J. Burdette	Louisiana State Univ. Sch. of Med.
David S. Carroll	Univ. of Tennessee College of Med.
Francis W. Chambers	Naval Medical Research Institute
William E. Cornatzer	Bowman Gray School of Medicine
C. L. Crispell	University of Virginia
Eugene P. Cronkite	Naval Medical Research Institute
Robert L. Driver	Medical College of Alabama
James C. Drye	Univ. of Louisville Sch. of Med.
Horace C. Dudley	Naval Medical Research Institute
Harry H. Dunham	Univ. of Kansas Medical Center
George A. Emerson	Univ. of Texas Medical Branch
John H. Ferguson	Univ. of North Carolina Med. Sch.
Gilbert H. Fletcher	M. D. Anderson Hospital, Houston
Herbert Francis	Vanderbilt Univ. Sch. of Medicine
Robert W. Gardier	Univ. of Tennessee College of Med.
C. E. Gardner	Duke University Sch. of Medicine
Joseph Gast	Baylor Univ. School of Medicine
W. Arnold Griswold	Univ. of Louisville Sch. of Med.
Arthur C. Guyton	University of Mississippi
W. F. Hamilton	University Hospital, Augusta, Ga.
Philip Handler	Duke Univ. School of Medicine
Clyde T. Hardy, Jr.	Bowman Gray Sch. of Medicine
James D. Hardy	Univ. of Tenn. College of Med.
Jerome S. Harris	Duke Univ. Sch. of Medicine
William N. Harsha	Univ. of Kansas Medical Center
John C. Hawk	Med. College of South Carolina
E. Byrom Hay	Baylor Univ. School of Medicine
Edward M. Hedgpeth	University of North Carolina
Reid Thomas Holmes	Bowman Gray Sch. of Medicine
S. Grant Holmes	Univ. of Texas Medical Branch
Margaret W. Holt	New England Deaconess Hosp., Boston
Joseph L. Irvin	University of North Carolina
Coleman Jacobson	Univ. of Pennsylvania
Cornelius T. Kaylor	Univ. of North Carolina Sch. of Med.
E. Richard King	U. S. Naval Hospital, Bethesda
J. Murray Kinsman	Univ. of Louisville Sch. of Med.
Charles F. Kittle	Univ. of Kansas Medical Center
Hampden C. Lawson	Univ. of Louisville Sch. of Med.
William C. Levin	Univ. of Texas Medical Branch
Alys H. Lipscomb	Univ. of Tenn. College of Med.
Champ Lyons	Medical College of Alabama
Isadore Meschan	Univ. of Arkansas Sch. of Med.
George R. Minor	University of Virginia Hospital
William G. Morgan	University of North Carolina
Joseph L. Morton	Ohio State University Hospital
Paul J. Murison	Ochsner Clinic, New Orleans
F. D. Murphy	Univ. of Kansas Medical Center
K. P. McConnell	Univ. of Texas Medical Branch
William M. McCord	Medical College of South Carolina
C. M. Norfleet, Jr.	Bowman Gray School of Medicine
William E. Nunnery	Bowman Gray School of Medicine
C. E. Nurnberger	Univ. of Tenn. College of Med.
H. Rowland Pearsall	Univ. of Virginia Dept. of Med.
Elbert L. Persons	Duke Univ. School of Med.
Everett L. Pirkey	Univ. of Louisville Sch. of Med.
R. W. Postlethwait	Medical College of South Carolina
Francis E. Ray	University of Florida
Allen F. Reid	Southwestern Medical College
William H. Riser	Medical College of Alabama
Arthur Roe	University of North Carolina
Wayne Rundles	Duke Univ. School of Medicine
S. M. Seidlin	Montefiore Hospital, New York
David Shapiro	University of Louisville
William W. Shingleton	Duke Univ. School of Med.
Ralph W. Stacy	Ohio State University
K. M. Stevens	Lynchburg, Va.
Howard G. Swann	Univ. of Texas Medical Branch
Robert S. Teague	Medical College of Alabama
Galen M. Tice	Univ. of Kansas Med. Center

III. Research Participants

Jack H. Brown	University of North Carolina

Charles H. Eades	University of Tennessee
Aaron Ganz	University of Tennessee
Perry M. Johnston	University of Arkansas
Robert C. Little	University of Tennessee
Joseph T. Lynn	North Carolina State College
Jasper Richardson	M.D. Anderson Hosp., Houston
John A. Sealander	University of Arkansas
Carroll A. Swanson	Ohio State University
John B. Whitney	Clemson College
John L. Wood	University of Tennessee

IV. Resident Physicians

John E. Wear	Duke University
Dana R. Schmidt	Henry Ford Hospital
Robert Owens	University of Kansas
Roderick J. Humphries	University of Texas Med. Branch
Edwin C. Bauer	University of Tennessee
Grey B. Kornegay	U. S. Marine Hospital
Max I. Miller	University of Kansas
Robert L. Pedersen	Duke University
Aubrey T. Hornsby	Duke University
Chiyeko Okawa	Medical College of Ala.
J. Earl Holmes	University of Louisville

V. Nursing Staff

Lucy M. Amburn
Jean Alice Anderson
Ruth E. Anthony
Roberta B. Clouser
Mary Nell Craig
Patricia Ann Fisher
Jessie A. Gnezda
Geneva Hefner
Vern A. Harrison
Mildred Miller
Peggy C. Moyers
Buena Pack
Sarah V. Robinson
Margie Lee Ross
Elsie P. Ruggles
Verda L. Wells

APPENDIX IV

SPECIAL TRAINING DIVISION

I. Consultant to Special Training Division

Cyril L. Comar	University of Tennessee - AEC Ag. Research Program

II. Lecturers Assisting in Training Program

Paul C. Aebersold	Atomic Energy Commission
Elda E. Anderson	Oak Ridge National Lab.
James Arnold	Argonne National Laboratory
Leonard F. Belanger	Univ. of Ottawa, Canada
Oscar Bizzell	Atomic Energy Commission
Harvey Blank	University of Pennsylvania
Rita Bogoroch	McGill Univ., Montreal, Canada
Cyril L. Comar	Univ. of Tenn. - AEC Ag. Research program
N. M. Dismuke	Oak Ridge National Laboratory
B. M. Drucker	Oak Ridge National Laboratory (Oak Ridge Graduate Fellow)
Robert A. Dudley	Mass. Institute of Technology
Patrick Fitzgerald	Sloan-Kettering Institute
D. A. Flanders	Argonne National Laboratory
John Gallimore	Oak Ridge Inst. of Nuclear Stu.
J. W. Givens	University of Tennessee Oak Ridge National Laboratory
Henry Gomberg	University of Michigan
Frank E. Hoecker	University of Kansas
Alexander Hollaender	Oak Ridge National Laboratory
Margaret Holt	New England Deaconess Hosp.
A. S. Householder	Oak Ridge National Laboratory
C. P. Leblond	McGill Univ., Montreal, Canada
S. Allen Lough	Atomic Energy Commission
William Lotz	Univ. of Tenn. - AEC Ag. Research Program
Walter S. Lundahl	Michigan State College
George Manov	Atomic Energy Commission
Rod Mason	Atomic Energy Commission
J. P. Nash	University of Illinois
S. R. Pelc	Hammersmith Hosp., London, E
C. L. Perry	Oak Ridge National Laboratory
D. V. L. Smith	Office of Naval Research
John Spence	Eastman Kodak Company
Daniel Steinberg	National Heart Institute
A. H. Taub	University of Illinois
Julian Webb	Eastman Kodak Company
John von Neumann	Institute for Advanced Study
Agnes Williams	Lovelace Clinic
George A. Boyd	Oak Ridge Inst. of Nuclear Stu. Univ. of Tenn. - AEC Ag. Research Program

III. Radioisotope School Participants

Twenty-second Course

Noel F. Bartone	New York Medical College
Jere M. Bauer	University of Michigan
Nels R. Benson	State College of Washington
James N. Bierly	Jefferson Hospital, Philadel
Albert Doerschuk	Amer. Cyanamid Co., Pearl R
Louis J. Eisele	Spring Hill (Ala.) College
Robert C. Frost	Rice Institute
Marvin B. Gillis	Internat'l Res. & Dev. Labs., Ft. Belvoir, Va.
Amelie Grauer	Brooklyn Polytechnic Instit
Charles E. Green	Engr. Res. & Dev. Labs., Ft. Belvoir, Va.
Vincent R. Grieco	New York Medical College
Mark A. Hayes	University of Mich. Med. Sch
Paul E. Hodgson	University of Mich. Med. Sch
Roderick J. Humphreys	University of Texas Med. Br
Robert M. Kallo	Fresno (Calif.) State College

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OAK RIDGE INSTITUTE OF NUCLEAR STUDIES

SEVENTH

ANNUAL REPORT

for the year ending JUNE 30, 1953

Medical Division

THE major development in the Medical Division during the year was the establishment of the Teletherapy Evaluation Board, whose aim is to examine the most promising isotopes as externally-administered radiation sources. The Board was organized and a prototype machine was under construction at year's end.

The Division continued during the year its extensive research on the use of gold-198 to reduce effusions resulting from carcinomas in the abdominal and peritoneal regions. It considerably extended its study of other colloids and biologically-inert complexes, fields of increasing importance in view of the generally disappointing results of metabolic substances (iodine being a rare exception).

A general review of the Division's activities during the year is set out below.

INTERNALLY-ADMINISTERED ISOTOPES

The Division initiated a study of the use of chromic phosphate to determine its value in radiation therapy. Animal studies showed retention on the pleural surfaces of a high percentage of injected material. Phosphorus-32 is a beta-emitter, a desirable characteristic when radiation of serous surfaces is sought. Gold, in contrast, emits gamma as well as beta rays. Following completion of animal tests, chromic phosphate was used in a limited number of patients, and studies of this isotope are continuing.

In addition to the colloids, the Division is studying other chemical methods of introducing biologically inert materials as carriers for radiation. Yttrium-90 has been used as an isotonic solution of a neutral salt of a heavy metal, the hyroxide of which has a low solubility product and reacts with tissue fluid to produce materials which are relatively inert biologically. Studies of intrapleural distribution in rats showed that 95 per cent of the total recovered dose remained in the space into which it was injected. Yttrium-90 is a beta emitter of 2.18 mev with no gamma rays.

The Division is in the preliminary stages of a testing program of leutecium-177. Leutecium is one of the rare earths of the lanthanide series, is commerically difficult to obtain, and is expensive, but merits testing. It has a half-life of 6.8 days and emits both gamma and beta rays at considerably lower energy levels than prevail with gold-198.

The program to investigate the value of gallium-67 in the study and possible treatment of osteoblastic types of bone lesions, either primary or metastatic, continues. A cooperative study is being made with the University of Virginia Department of Surgery to determine the criteria for resecting pulmonary metastases at the same time that uptake studies with tracer doses of gallium are being made.

Distribution of antimony given as a trivalent organic complex has been studied in a small number of patients. Much of the isotope was deposited in the liver, which might suggest that it behaves as a colloid, but in other respects distribution was quite different from the colloid pattern. There was rather large deposition in the kidney, and studies on rats demonstrate a rather striking deposition of antimony in the red cells. Later tests indicated that deposition was in the protein portion of the hemoglobin. Incidental observations in the animal studies included a high concentration of antimony in the pituitary glands of rats eight days after injection, and higher concentrations in the cortex than in the medulla of kidneys of dogs.

The Medical Division by now has an extensive backlog of experience in the use of radioactive gold, and basic studies of the distribution and metabolism of colloidal radiogold are being continued. Autoradiographic distribution has been determined in rats after intravenous administration of low and high doses. Through the three-year period in which this isotope has been used, special efforts have been made to obtain hematologic information following its use. Further information on blood and bone marrow changes is being assembled to evaluate the general pattern of response. The route of administration of the isotope appears to make a great deal of difference in the degree of hematologic effect.

A number of patients were studied after receiving injections of intravenous radioactive colloidal gold. Two of these were in individuals in whom it was hoped that some therapeutic effect might be obtained for carcinoma of the liver. Several of the others were individuals with advanced neoplastic diseases to whom the isotope was given shortly before death. The colloidal gold was seen to deposit in the liver to a very large extent and the deposition was quite uniform in areas where the liver parenchyma was unimpaired by vascular damage or cellular infiltration. Areas of damaged liver showed a less uniform concentration. Areas of metastatic neoplasm in the liver were notably lacking in any ability to take up the colloidal material. Utilizing this information, the Division has attempted to locate metastatic lesions in the liver on the basis of a lack of concentration of the isotope in these areas.

On the basis of animal work done by Harold Berg, M.D., and his associates at Louisville in conjunction with the Medical Division, clinical studies are now under way with colloidal gold-198 given by intrabronchial injection at the time of bronchoscopy. It appears that in dogs it is possible to obtain an intense radiation of mediastinal lymph nodes by this method.

Interest in iodine-131 in thryoid disease has continued with further clinical studies on patients with malignant and benign lesions. One special reason for continued interest is the importance of teaching residents the more routine and widely-used isotope procedures. Further data on histologic changes in normal thryoid tissue after therapeutic doses of iodine-131 has been accumulated, and well-correlated studies in dogs have been made.

In addition to its basic and clinical studies, the Medical Division also has under study a number of approaches to improving or simplifying radiochemical analysis.

A chemical method of dosage determination is being developed to provide better information on integral dosage in therapeutic applications of isotopes. The paper chromatographic technique is being utilized to study iodine-containing compounds in the human body.

A device called a Scintiscanner has been installed to provide an additional means of recording the location of isotopes inside the body. This unit includes a collimated scintillation counter mounted in such a way that it will survey a given area and by a series of impulses record the degree of radioactivity within that area by the frequency of its response.

Several members of the Medical Division staff are studying fundamental problems related to the therapeutic program. One of these is a study of serous effusions utilizing iodinated human serum albumin and measuring its disappearance from the blood and peritoneal cavities in patients with ascites. A study of the effect of ACTH on eosinophil count in peripheral blood and bone marrow is under way.

TELETHERAPY EVALUATION PROGRAM

The Teletherapy Evaluation Program is a joint effort by the Institute Medical Division and 20 participating medical schools to develop a variety of teletherapy units useful in the treatment of cancer. A Teletherapy Evaluation Board consisting of representatives of each of the cooperating institutions is now actively engaged in the conduct of the program. The board is broken down into an executive committee and six subcommittees. The executive committee exercises general supervision of the entire program. Members of the subcommittees concern themselves with specific aspects of the program. Subcommittees and their memberships are as follows:

Executive Committee

Robert J. Reeves, M.D.	Duke University
H. D. Kerman, M.D.	University of Louisville
C. C. McClure, M.D.	Vanderbilt University
Sidney Rubenfeld, M.D.	New York University - Bellevue Medical Center
Galen M. Tice, M.D.	University of Kansas
Marshall Brucer, M.D.	Oak Ridge Institute of Nuclear Studies

Subcommittee No. 1--Source Evaluation and Shield Design

Frank Hoecker	University of Kansas
H. D. Kerman, M.D.	University of Louisville
David S. Carroll M.D.	University of Tennessee
H. Stephen Weens, M.D.	Emory University
John Tolan	Emory University
Carl E. Nurnburger	University of Tennessee
Marshall Brucer, M.D.	Oak Ridge Institute of Nuclear Studies

Subcommittee No. 2--Small Source Design

Henry Jaffe, M.D.	University of Southern California
Robert J. Reeves, M.D.	Duke University
Paul Riemenschneider, M.D.	University of Syracuse
John Tolan	Emory University
C. C. McClure, M.D.	Vanderbilt University
J. F. Kelly, Jr., M.D.	University of Nebraska
Marshall Brucer, M.D.	Oak Ridge Institute of Nuclear Studies

Subcommittee No. 3--Rotational Methods and Procedures

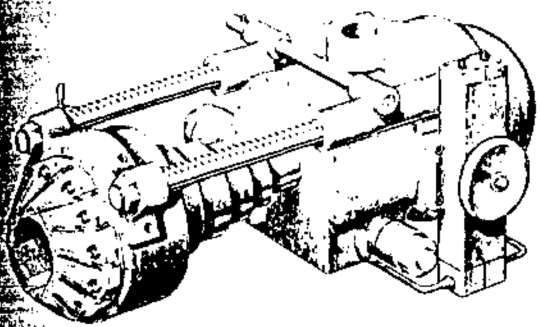
Sidney Rubenfeld, M.D.	New York University - Bellevue Medical Center
Arthur C. Guyton, M.D.	University of Mississippi
William H. Riser, M.D.	Medical College of Alabama
Carl E. Nurnburger	University of Tennessee
George Cooper, M.D.	University of Virginia
Marshall Brucer, M.D.	Oak Ridge Institute of Nuclear Studies

Subcommittee No. 4--Housing Design

Frank E. Hoecker	University of Kansas
James E. Lofstrom, M.D.	Wayne University
Frederick Mandeville, M.D.	Medical College of Virginia
Walter J. Burdette, M.D.	Louisiana State University
Galen M. Tice, M.D.	University of Kansas
J. Robert Andrews, M.D.	Bowman Gray School of Medicine

Subcommittee No. 5--Clinical Program

C. C. McClure, M.D.	Vanderbilt University
J. Robert Andrews, M.D.	Bowman Gray School of Medicine



"Head" of Teletherapy Unit

rotational patterns for the beam and has been designed so as to use cobalt, europium, or cesium as the radiation source. Because of its availability, cobalt-60 will be used initially as the radiation source. The unit is expected to be installed and placed in operation in the Medical Division in the early spring of 1954.

After a program of preliminary testing with this unit, it is expected that a simplified design involving an adequate but reduced variety of rotational patterns will be agreed upon by the board. It is expected that several of the medical schools represented on the board will then procure units of this modified design and use them in a large-scale cooperative clinical evaluation program. The proposed basis for use involves the utilization of each unit 25 per cent of the time for the clinical program established by the Teletherapy Evaluation Board with the remaining 75 per cent of the time on each unit available to the regular research and therapy programs of the separate schools.

The board through one of its subcommittees has also devoted itself to the design of a non-rotational low curiage cobalt-60 unit for use primarily in head and neck irradiations. A major design objective for this unit is that it should sell competitively with the conventional 250 KV x-ray units now widely used for deep radiation therapy. It is expected that a number of the medical schools represented on the board will procure such units when they become available and will cooperate in their clinical evaluation in a program specified by the board on the same basis as that proposed for the rotational unit.

Each of the 22 participating medical schools is contributing $2,500 to the Teletherapy Evaluation Program. This is expected to represent about 25 per cent of the total cost of the program, with the remainder supplied by the Institute from funds reimbursable by the Atomic Energy Commission.

The Teletherapy Evaluation Board was organized at a meeting of medical school representatives at Oak Ridge on August 8, 1952, following approval of the outlines of the program by the Institute Council and Board of Directors. The subcommittees meet as the progress of the program requires. The entire teletherapy board is not expected to meet oftener than once a year. The executive committee, on the other hand, has already held several meetings.

COBALT-60 IRRADIATOR

The Medical Division completed its phase of the joint program with the University of Texas-M. D. Anderson Hospital to develop a cobalt-60 irradiator. The housing for the irradiator was delivered by the General Electric Company, in November, 1951. Since the high-level source was still not available from the Canadian reactor at Chalk River, the unit was loaded with a 220-curie source at Oak Ridge National Laboratory, and loaned to the Institute by Max Cutler, M.D., then of the Chicago Tumor Institute. This source was loaded into the housing by the Laboratory and used until the arrival of the 800-curie source from Chalk River in July, 1952. This source also was loaded at the Laboratory and since that time a wide range of tests has been run to characterize the radiation beam. This phase of the program was complete, and the unit was ready to transfer to the M. D. Anderson Hospital at year's end.

CARE OF PATIENTS

The Medical Division last year accepted 148 patients for treatment, in addition to a considerable number seen as out-patients, with a census of 5,527 patient days. This was the largest annual number of patients to be accepted by the Division. In the three previous years, the Division had accepted a total of 202 patients. The accompanying chart shows the origin by state of patients.

A series of developments extending over the years has greatly improved the facilities for the general care of patients. An outdoor plaza has been built, patient rooms now are fully air-conditioned in the summer months, and an occupational therapy program is carried out. A number of Oak Ridge groups have undertaken special projects to improve patient morale and well-being.

A number of Oak Ridge's medical practitioners have given invaluable assistance in the conduct of the Medical Division program, particularly in the care of patients. These include the Oak Ridge Hospital radiologist, Robert Ball, M.D., who is participating actively in the Teletherapy Evaluation Program; and Drs. R. R. Bigelow, Dexter

Davis, Raymond A. Johnson, Dana W. Nance, C. J. Speas, and Paul Spray.

ADMISSIONS TO ORINS RESEARCH HOSPITAL

States	All Previous Years	7/1/52-6/30/53	Total Admissions
Alabama	16	7	23
Arkansas	3	3	6
California	1	0	1
Florida	1	17	18
Georgia	7	3	10
Indiana	1	2	3
Iowa	1	0	1
Kansas	1	1	2
Kentucky	36	13	49
Louisiana	4	2	6
Maryland	1	0	1
Michigan	1	0	1
Mississippi	5	0	5
Missouri	9	0	9
North Carolina	28	12	40
New Mexico	1	0	1
New York	0	1	1
Ohio	2	0	2
Pennsylvania	2	0	2
South Carolina	11	6	17
Tennessee	64	54	118
Texas	5	2	7
Virginia	13	15	28
23 states	202	149	351

Total patient days from July 1, 1953, through June 30, 1953: 5,527

TRAINING PROGRAM

The Medical Division continued its regular resident training program during the year, with 17 residents (including 7 from the Air Force) accepted for three-month periods. An important addition to the training program has been the establishment of two one-year residencies in experimental medicine, although these posts have not yet been filled. These residencies have been approved for basic credit in internal medicine by the American Medical Association and the American Board of Internal Medicine. Yearly stipend of $2,000 plus $4.00 a day subsistence in lieu of maintenance is provided.

Members of the Medical Division staff spoke at 12 professional meetings during the year. Professional visitors to the Division numbered 251.

The Division staff also assists in the conduct of the radioisotope techniques courses given by the Special Training Division, assuming responsibility for those portions of the courses dealing with medical uses of isotopes.

ISOTOPES USED BY THE MEDICAL DIVISION

Isotope	Total F.Y. 1953 Curies	Total for Previous Years Curies
Antimony-122,124	0.512*	2.75
Calcium-45	0.001	—
Carbon-14	—	0.011
Cesium-137	2.000	—
Cobalt-56,57	—	0.01
Cobalt-60	1.250	12.92
Copper-64	0.100	—
Europium-152,154	—	2.000
Gallium-67	2.148	0.84
Gallium-72	—	13.87
Gold-198	13.012	24.91
Gold (pellets)	0.950	—
Hafnium-181	6 units	10.15
Iodine-130	1 (bombardment)	—
Iodine-131	1.400	5.9
Iodo-albumin	0.036	—
Iodine-131, thyroxine	0.003	—
Iridium-192	—	0.200
Iron-59	0.001	—
Lutecium-177	0.096	—
Manganese-54	—	0.011
Molybdenum-99	0.001	—
Nickel-63	—	0.003
Phosphorus-32	0.365	0.21
Phosphorus-32 (plaques)	100,000 (Rep.)	—
Potassium-42	0.013	0.033
Ruthenium-103	—	0.05
Sodium-24	0.001	0.75
Sulfur-35	0.040	0.261
Yttrium-91	0.005	—
Zirconium-95	—	0.001

PUBLICATIONS FROM THE MEDICAL DIVISION (FISCAL YEAR 1953)

DESIGN AND CONSTRUCTION OF A MULTI-CURIE COBALT TELETHERAPY UNIT. L. G. Grimmett, H. D. Kerman, M. Brucer, G. H. Fletcher, and J. E. Richardson. *Radiology*, Vol. 59, No. 1, July 1952.

*15.6 mc Sb-122 per shipment as calculated
0.4 mc Sb-124 from estimated specific activity

BLOOD-CLOTTING STUDIES ON DOGS INTERNALLY IRRADIATED WITH RADIOGOLD. J. H. Ferguson, G. A. Andrews, and M. Brucer. *Proceedings of the Society For Experimental Biology And Medicine*, Vol. 80, July 1952.

THE EFFECT OF PARTICLE SIZE ON BLOOD CLEARANCE AND TISSUE DISTRIBUTION OF RADIOACTIVE GOLD COLLOIDS. D. B. Zilversmit, G. A. Boyd, and M. Brucer. *The Journal Of Laboratory And Clinical Medicine*, Vol. 40, No. 2, August 1952.

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THE BILIARY EXCRETION OF GALLIUM-72, GOLD-198, AND HAFNIUM-181 IN THE RAT. J. W. Archdeacon, J. B. Nash, and G. C. Wilson. *Texas Reports On Biology And Medicine*, Vol. 10, No. 2, Summer 1952.

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THE POSSIBILITIES AND LIMITATIONS OF ISOTOPE THERAPY OF CANCER. G. A. Andrews. *The Journal Of The Kansas Medical Society*, Vol. 53, No. 12, December 1952.

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SHAPED SOURCES FOR TELETHERAPY UNITS. M. Brucer, W. G. Pollard, H. Leiter, and H. Scarf. *Nucleonics*, Vol. 11, No. 2, February 1953.

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INTRACAVITARY COLLOIDAL RADIOGOLD IN THE TREATMENT OF EFFUSIONS CAUSED BY MALIGNANT NEOPLASMS. G. A. Andrews, S. W. Root, H. D. Kerman, and R. R. Bigelow. *Annals Of Surgery*, Vol. 137, No. 3, March 1953, pages 375-381.

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EFFECT OF ACTH ON THE EOSINOPHIL COUNT IN PERIPHERAL BLOOD AND BONE MARROW. S. W. Root and G. A. Andrews with

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the technical assistance of E. Hodgens. *American Journal Of Medicine.*

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ACCEPTED FOR PUBLICATION

A STUDY OF GALLIUM-72 BY THE STAFF OF THE ORINS MEDICAL DIVISION. *Radiology.*

EFFECT OF CHAMBER VOLTAGE ON ELECTRON BUILD-UP MEASUREMENTS. J. E. Richardson. *Radiology.*

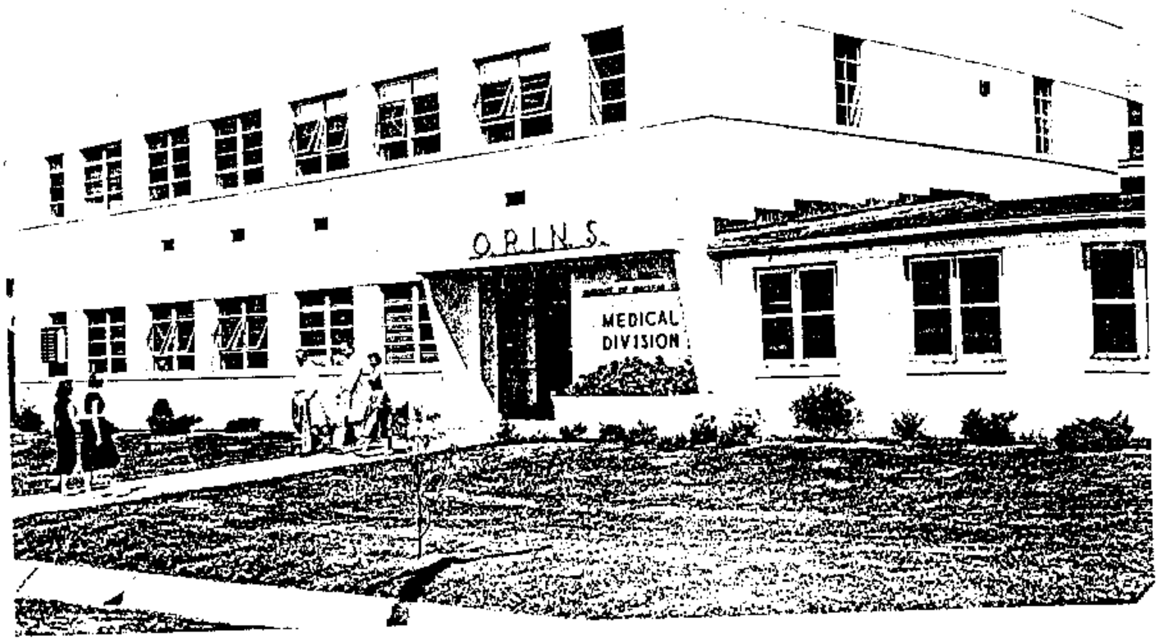
INTRACAVITARY USE OF COLLOIDAL RADIOACTIVE GOLD. G. A. Andrews, S. W. Root, R. M. Kniseley, and H. D. Kerman. *Radiology.*

SUBMITTED FOR PUBLICATION

POSSIBILITIES OF USING THE (n, α) REACTION TO STUDY THE DISTRIBUTION OF BORON IN TISSUES. Giovanna Mayr, H. D. Bruner, and M. Brucer. *Nucleonics.*

AUTORADIOGRAPHIC DISTRIBUTION OF INTRAVENOUS COLLOIDAL GOLD (AU-198) IN THE RAT. V. A. Stembridge, R. M. Kniseley, and W. Gibbs. *Laboratory Investigation.*

HAFNIUM COMPLEXES FOR BIOLOGICAL INVESTIGATION. E. Macdonald and C. T. Bahner. *The Proceedings Of The Society For Experimental Biology And Medicine.*



Institute Medical Division

APPENDIX I

PERSONNEL OF THE OAK RIDGE INSTITUTE OF NUCLEAR STUDIES

(as of July 1, 1953)

H. Morgan	A & M College of Texas
llison	Alabama Polytechnic Institute
Herzfeld	Catholic Univ. of America
Hunter	Clemson Agricultural College
Nielsen	Duke University
M. Phillips	Emory University
Carothers	Florida State University
Sweigert	Georgia Institute of Technology
Keen	Louisiana State University
Etheredge	Mississippi State College
Beck	North Carolina State College
Bonner	Rice Institute
Nieset	Tulane University of Louisiana
ten Hoor	University of Alabama
Grigorieff	University of Arkansas
Eutsler	University of Florida
Boyd	University of Georgia
Dawson	University of Kentucky
Ernst	University of Louisville
ld Bamford	University of Maryland
McCarter	University of Mississippi
D. Van Cleave	University of North Carolina
H. Wender	University of Oklahoma
ndo Bueso	University of Puerto Rico
W. Davis	University of South Carolina
A. Waters	University of Tennessee
lcolm Y. Colby	University of Texas
H. Yoe	University of Virginia
D. Peterson	Vanderbilt University
A. Vilbrandt	Virginia Polytechnic Institute

B. Board of Directors

Paul Magnus Gross, *President*
Vice President, Duke University

Jesse Wakefield Beams, *Vice President*
Professor of Physics, University of Virginia

George Hugh Boyd, *Director & Chairman of the Council*
Dean of the Graduate School, University of Georgia

John Ray Dunning, *Director*
Dean of Engineering, Columbia Univ.

William Vermillion Houston, *Director*
President, Rice Institute

Samuel Colville Lind, *Director*
Technical Advisor, Carbide & Carbon Chemicals Company, Oak Ridge

Hayden Coler Nicholson, *Director*
Dean, School of Medicine, University of Arkansas

Theophilus Shickel Painter, *Director*
President, University of Texas

Louis Arthur Pardue, *Director*
Vice President, Virginia Polytechnic Institute

sonnel

OFFICE OF THE EXECUTIVE DIRECTOR

William G. Pollard, Executive Director

George B. Pegram, Consultant

J. DeLozier	Secretary
een V. Denis	Secretary
Ethridge	Record Clerk
L. Fletcher	Record Clerk
Garber	Librarian
Halburnt	Record Clerk
Ison	Record Clerk
Johnson	Hd., Info. Dept.
Lewis	Secretary-Senior
ise Markel	Librarian
yce McIlhenny	Info. Asst.
V. Mumford	Assistant Treasurer
Rutherford	Auditor
inhold Schlueter	Library Supv.

OFFICE OF ADMINISTRATION

Paul M. Elza, Manager of Administration

Jess F. Benton	Accountant
William Blankenship	Maint. Mech. I
George N. Brent	Inst. Engineer
Ralph B. Briggs	Maint. Mech. II
John Burns	Helper (temp.)
Daniel W. Capps	Procedures Asst. (temp.)
Joan R. Clouse	Stenographer
Barbara Cole	Stenographer
Paul G. Davis	Storekeeper
Charles H. Day	Stockkeeper
W. G. Disney	Accounting Clerk
Harrison E. Elliott	Purchasing Agent
Ellen Epperson	Accountant
John H. Fenton	Hd., Manag. Serv. Dept.
Dewey Ferguson	Maint. Mech. I
Virginia Gilpatrick	Record Clerk
Walter Graves	Maint. Mech. II

Barbara Guinn	Clerk-Typist
Johnnie Harvest	Helper (temp.)
Nathaniel Hill	Inst. Engineer
Joseph Houston	Photographer
Billie Hurt	Clerk-Typist (temp.)
Carl E. Johnson	Maint. Mech. I (temp.)
Faye J. Jones	Clerk-Typist
Harry E. Kimble	Instrument Maker
Arch E. Long	Maint. Mech. II
Kaye Margrave	Clerk-Typist
T. W. Martin	Hd., Tech. Serv. Dept.
Barbara McClannahan	Section Supervisor
Dorothy Nanney	Accounting Clerk
Arville R. Nelson	Maint. Mech. I
William Perry	Mail Clerk
Billy J. Pitts	Helper (temp.)
William Rhodey	Maint. Mech. II
J. W. Rose	Hd., Fiscal Serv. Dept.
Jenny Rose	Clerk-Typist
Gloria Roseberry	Vari-Typist
H. J. Russell	Maint. Mech. I
Mary E. Russell	Section Supervisor
Wendell Russell	Management Asst.
W. D. Schwartzman	Property & Supply Asst.
*William L. Scott	Mech. Engr.
Amon D. Silcox	Maint. Mech. I (temp.)
Hugh Simpson	Custodian
Rosella Stooksbury	Receptionist
Robert Taylor	Delivery Man
Marvin Triplett	Section Supv.
Mavis Uthe	Clerk-Typist
Nancy Vail	Record Clerk
Johnny Vaughn	Helper
Leonard Vickery	Helper
Decatur M. Walker	Inst. Maker (temp.)
Lendell Z. Walker	Helper (temp.)
Charles Wallace	Cabinet Maker
James Wilde	Instrument Engineer
Robert Youngblood	Maint. Mech. II

UNIVERSITY RELATIONS DIVISION

Russell S. Poor, Chairman

Marion T. Clark	Asst. and Acting Chairman
Frances A. Crowley	Stenographer
William Dryden	Admin. Asst.
Ann Hicks	Stenographer
Trula Hobbs	Secretary
Nelle Strange	Fellowship Asst.

MEDICAL DIVISION

Marshall Brucer, Chairman

Lucy M. Amburn	Nurses Aide
Ugo Amelio	Lab. Asst.
Elizabeth B. Anderson	Research Assoc.
Gould A. Andrews	Chief, Clin. Services
Harold E. Bishop	Lab. Tech.
William R. Buher	Research Asst.
Betty M. Cooper	Sr. Scientist
Gladys E. Cooper	Nurse-Gen. Duty
Henry P. Copeland	Lab. Tech.
Roberta B. Clouser	Staff Nurse
Mary N. Craig	Staff Nurse
Edgar A. Cress	Research Asst.
John H. Dean, Jr.	Orderly
John W. Deathriadge	Custodian (Military Leave of Absence)
Rachel C. Dixon	Lab. Aide
Lewis Dobson	Helper
Timothy Dowdell	Helper
Nelda Edwards	Tech. Secretary
James Eldridge	Research Assoc.
William C. Fields	Lab. Tech.
Dorothy L. Finley	Stenographer
Patricia Fisher	Nurse-Gen. Duty
Eula B. Francis	Stenographer
William D. Gibbs	Lab. Tech.
Bobbie Jean Giovannucci	Nurse-Gen. Duty (temp.)
Betty C. Gray	Lab. Tech.
Joe Gray	Research Assoc.
J. H. Harmon	Admin. Officer
Raymond L. Hayes	Scientist
Geneva Hefner	Nurses Aide
Eva Hodgens	Res. Tech.
George R. Holloway	Orderly
Mabel Hurst	Med. Records Librarian
Mary S. Hyder	Nurse-Gen. Duty
Edith K. Kees	Nurses Aide
Elmer L. Keller	Lab. Tech.
Mary M. Knight	Lab. Tech.
Ralph M. Kniseley	Prin. Scientist
Granvil Kyker	Prin. Scientist
Vivian D. Lay	Clerk-Typist
Clara J. Leslie	Nurse-Gen. Duty (Leave of Absence)
William C. Martin	Lab. Asst.
Evan D. McKissic, Jr.	Custodian
Margie R. Meeks	Nurses Aide
Peggy C. Moyers	Nurse-Gen. Duty
*Priscilla A. Oliver	Occup. Therapist
Beuna Pack	Nurses Aide
Mattie Bell Perry	Custodian
Naomi D. Presnell	Nurse-Gen. Duty
Blanche Richardson	Record Clerk
Sarah V. Robison	Nurse-Gen. Duty
*Samuel Root	Clinician
John C. Rowland	Custodian
Elsie P. Ruggles	Nurse-Gen. Duty
Edward M. Russ	Lab. Tech.
*Marie Scharl	Nurses Aide
Lillie P. Simmons	Custodian
*Mary P. Smyser	Lab. Tech.
Barbara H. Stevens	Nurse-Gen. Duty
Martha G. Stewart	Lab. Tech.
Mary Sutliff	Nurse-Supv.
Elizabeth L. Thomas	Lab. Asst.
Malcolm P. Tyor	Clinician
Elmer L. Warren	Lab. Tech. (temp.)
James O. White	Orderly (Military Leave of Absence)

*Part-time employees

SPECIAL TRAINING DIVISION

Ralph T. Overman, Chairman

George A. Boyd	Sr. Scientist
Izziah Jones	Custodian
Myron S. McCay	Instructor (temp.)
Elizabeth Rona	Sr. Scientist
John N. Sams	Lab. Asst.
Margaret L. Scott	Clerk-Typist
Frances Smellage	Secretary
Donald R. Smith	Scientist
Ardell C. Stewart	Lab. Tech.
Edith Wilson	Secretary

EXHIBITS DIVISION

David L. DeJarnette, Chairman

Lonnie W. Austin	Maintenance Mech. I
Mary S. Bowman	Helper (temp.)
*Charles S. Davis	Museum Aide
W. Earl Duff	Admin. Asst.
Willie H. Dunn	Maint. Mech. I
Jean E. Fahey	Receptionist
Wheeler Fain	Custodian
John N. Fox	Exhibits Manager
Renfro Henderson	Custodian
Jack D. Johnson	Museum Asst.
Robert R. McDonald	Maint. Mech. I
Alice N. Montgomery	Clerk-Typist
George B. Presley	Display Artist
Harold E. Price	Display Artist
Wm. C. Rinearson	Museum Aide
Theodore Robbins	Maint. Mech. I
Donald G. Robertson	Museum Asst.
Robt. C. Rothermel	Exhibits Manager
Larry H. Sharp	Exhibits Designer
Mary S. Tuccinardi	Secretary
Robt. G. Wells	Museum Aide
*Mary B. Woodward	Clerk-Typist

TERMINATIONS

OFFICE OF THE EXECUTIVE DIRECTOR

Mary Joy Clapp	Record Clerk
Betty R. Davis	Sr. Record Clerk
Madeline K. Lent	Sr. Record Clerk

OFFICE OF ADMINISTRATION

Fern C. Brewster	Clerk-Typist
Stanley W. Denny	Helper (temp.)
William Dumas	Helper
Zora H. Gimera	Secretary
Barbara J. Goss	Stenographer
Beatrice M. Holtzclaw	Clerk-Typist
Dorothy L. Johnson	Stenographer
Eleanor V. Munton	Secretary
Wm. R. Ramsay	Budget & Procedures Asst.
Henry Thomas	Maint. Mech. II
Chas. L. Vaughn	Chief, Maint. Mech.
*Donald D. Walker	Inst. Maker
Marjorie L. Whittlesey	Stenographer
Adelene Woodworth	Secretary

UNIVERSITY RELATIONS DIVISION

Vera E. Coffey	Stenographer
Donna M. Dinsmore	Record Clerk
Lesta H. Prater	Clerk-Typist

MEDICAL DIVISION

Jessie G. Almond	Nurse-Gen. Duty
Jean A. Anderson	Nurse-Gen. Duty
Ruth E. Anthony	Nurse-Gen. Duty
Mary C. Bondurant	Lab. Tech.
Janet H. Broad	Sr. Record Clerk
Elmer A. Carpenter	Custodian
Harold R. Case	Lab. Tech.
Hugh M. Dobson	Orderly
Robert J. Gibson	Lab. Tech.
Elmer A. Greene	Research Tech.
Vern A. Harrison	Nurse-Gen. Duty
Anna R. Henley	Custodian
Morris C. Holmes	Custodian
*Dorothy L. Kelly	Nurses Aide
Herbert D. Kerman	Principal Scientist
Wallace K. Luke	Lab. Tech.
Betty B. Magnusson	Lab. Tech. (temp.)
Francis G. McMahon	Lab. Tech. (temp.)
Mildred Miller	Nurse-Gen. Duty
Dorothy G. Osteen	Admin. Aide
Helen S. Randolph	Lab. Tech.
Mary E. Roberts	Clerk-Typist (temp.)
Mary K. Simpson	Custodian
Verda L. Wells	Nurse-Gen. Duty

SPECIAL TRAINING DIVISION

Joseph E. Eve	Lab. Aide
Ralph H. Firminhac	Scientist
Charles S. Simons	Sr. Scientist

EXHIBITS DIVISION

Margaret K. Brooks	Secretary
Edward S. Burnette	Museum Aide
Joseph B. Martin	Museum Aide

*Part-time employees

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Postdoctoral Fellows Studying Abroad

Bermuda Biological Station for Research
St. George's, Bermuda

Travis, Dorothy F.	L. W. Hutchins	George Wash. University	Biology

Cambridge University
Cambridge, England

Harbottle, Garman	A. G. Maddock	Calif. Inst. of Tech.	Radio-chemistry
Hintz, Norton M.	O. R. Frisch	Univ. of Cal. at Los Angeles	Physics

College de France
Paris, France

Corliss, John O.	E. Faure-Fremiet	University of Vermont	Biology

Leiden University
Leiden, Holland

Lynton, Ernest A.	C. J. Gorter	Carnegie Inst. of Technology	Physics

Max Planck Institut
Goettingen, Germany

Ferrell, Richard A.	W. Heisenberg	Calif. Inst. of Technology	Physics

University of Copenhagen
Copenhagen, Denmark

Mottelson, Ben R.	Niels Bohr	Purdue Univ.	Physics

APPENDIX III

MEDICAL DIVISION

I. Medical Advisory Panel

George T. Harrell, Chairman
Bowman Gray School of Medicine

R. Lee Clark	M.D. Anderson Hospital
Wilburt C. Davison	Duke University
Manuel Garcia	Tulane University of La.
Chalmers L. Gemmill	University of Virginia
Paul W. Schafer	University of Kansas
Douglas H. Sprunt	University of Tennessee

II. Consultants to the Medical Division

Alabama

University of Alabama Medical College
Champ Lyons
William H. Riser
Robert S. Teague

Arkansas

University of Arkansas School of Medicine
Isadore Meschan
Thomas Harold Oddie

California

University of Southern California School of Medicine
Henry L. Jaffe

Delaware

Memorial Hospital - Wilmington, Delaware
R. A. Neubauer

Florida

University of Florida
David Ellis
Francis C. Ray

Florida State Board of Health
Lorenzo Lynn Parks

Georgia

Emory University School of Medicine
Robert L. Brown
Harry D. Bruner
John H. Tolan
H. Stephen Weens
Alfred E. Wilhelmi

University of Georgia School of Medicine
Stephen W. Brown
Hoke Wammock

Kansas

University of Kansas
Frank E. Hoecker

University of Kansas Medical Center
Paul H. Lothan

University of Kansas School of Medicine
Charles Frederick Kittle
Franklin David Murphy
Galen M. Tice

Kentucky

Veterans Administration Hospital
David Shapiro

University of Louisville School of Medicine
Harold F. Berg
J. Ray Bryant
James C. Drye
R. Arnold Griswold
Herbert D. Kerman
J. Murray Kinsman
Hampden C. Lawson

Kenneth P. McConnell
Everett Pirkey

Louisiana

Louisiana State University School of Medicine

Walter James Burdette

Ochsner Clinic

William R. Arrowsmith
Paul J. Murison

Maryland

Naval Medical Research Institute

Eugene P. Cronkite

Michigan

University of Michigan School of Medicine

Jere Bauer

Wayne University College of Medicine

James E. Lofstrom
William E. Conrady

Mississippi

University of Mississippi School of Medicine

Arthur C. Guyton

Missouri

Ellis Fischel State Cancer Hospital

John C. Tinsley, Jr.

Nebraska

Creighton University School of Medicine

James F. Kelly, Jr.

University of Nebraska

Howard B. Hunt

New York

Francis Delafield Hospital

Carl B. Braestrup

Private Physician

S. M. Seidlin

Naval Medical Research Institute

H. C. Dudley

New York University - Bellevue Center

Sidney Rubenfeld

Syracuse Memorial Hospital

Paul A. Riemenschneider

North Carolina

Bowman-Gray School of Medicine

Jerry K. Aikawa
John R. Andrews
Camillo Artom
William E. Cornatzer
Charles M. Norfleet
Carolyn Haines Purdy
Ernest H. Yount

Duke University School of Medicine

William G. Anylan
Clarence Ellsworth Gardner, Jr.
Philip Handler
Jerome S. Harris
Harold W. Lewis
Robert J. Reeves
Wayne Rundles
William Shingleton

University of North Carolina

M. K. Berkut
John Howard Ferguson
Edward McGowan Hedgpeth
Joseph Logan Irvin
Cornelius T. Kaylor
William Gardner Morgan
Arthur Roe
Charles D. Van Cleave

Ohio

Ohio State University

Joseph L. Morton
Ralph W. Stacy
Claude-Starr Wright

South Carolina

State of South Carolina Medical College

John C. Hawk
William M. McCord

Tennessee

Carson Newman College

Carl T. Bahner

UT-AEC Agricultural Research Program

Cyril Comar

Vanderbilt University

Herbert Francis
C. C. McClure

Oak Ridge - AEC

Paul C. Aebersold

University of Tennessee College of Medicine

Ralph R. Braund
David S. Carroll
James Daniel Hardy
Alys H. Lipscomb
Carl E. Nurnberger
Jesse D. Perkinson, Jr.
John L. Wood
Robert A. Woodbury

Oak Ridge Hospital

Robert P. Ball
Robert R. Bigelow
Dana W. Nance
Paul E. Spray

Texas

Southwestern Medical College

Allen F. Reid

University of Texas Medical Branch

Charles R. Allen
Ludwik Anigestein
George Albert Emerson
William G. Levin
Joe Bert Nash
Wiktor Waclaw Nowinski
Martin Schneider
Vernie Albert Stembridge
Howard G. Swann

M. D. Anderson Hospital

Gilbert H. Fletcher

Baylor University School of Medicine

Joseph Gast
Elliott B. Hay
John A. Isherwood
Vincent Collins

Jefferson Davis Hospital

R. Kenneth Loeffler

Virginia

Medical College of Virginia

Frederick B. Mandeville
George Zur Williams

University of Virginia

George Cooper
Kenneth R. Crispell
George R. Minor

Puerto Rico

University of Puerto Rico

Lyndon E. Lee

Air Force Resident Physicians

Maj. W. H. Westbrook	Magnolia, Arkansas
Lt. David R. Moomaw	Maxwell Air Force Base Montgomery, Alabama
Maj. Robert L. Chancey	Lowery Air Force Base Denver, Colorado
Col. Osmo I. Niemi	Fort Totten Long Island New York City
Capt. F. W. Freeman	Wright Patterson Air Force Base Dayton, Ohio
Maj. Samuel R. Hill	Greensboro, North Carolina
Capt. Norman O. Harris	School of Aviation Medicine Randolph Field, Texas

III. Research Participants

Aaron Ganz	University of Tennessee Memphis, Tennessee
Robert C. Little	University of Tennessee Memphis, Tennessee
George Johnson	University of Arkansas Little Rock, Arkansas

IV. Resident Physicians

Etna Palmer	Bowman Gray School of Medicine Winston-Salem, North Carolina
Charles Montgomery	University of Kansas Kansas City, Kansas
Martin Levene	Massachusetts General Hospital Boston, Massachusetts
Shirley Rivers	Bowman Gray School of Medicine Winston-Salem, North Carolina
Louise Hutchinson	Tulane University New Orleans, Louisiana
Robert Hutchinson	Tulane University New Orleans, Louisiana
Wilma Jeanne Canada	Massachusetts General Hospital Boston, Massachusetts
Herbert B. Kelly	Tulane University New Orleans, Louisiana
Earl I. Holmes	University of Louisville Louisville, Kentucky
Joseph McAlister	Duke University Durham, North Carolina
Vernie A. Stembridge	University of Texas Galveston, Texas

V. Teletherapy Evaluation Board

Institution	Representative on TEB
Baylor University	Vincent Collins, M.D.
Creighton University	James F. Kelly, Jr., M.D.
Duke University	Robert J. Reeves, M.D.
Emory University	H. Stephen Weens, M.D.
Louisiana State Univ.	Walter J. Burdette, M.D.
Medical College of Virginia	Frederick B. Mandeville, M.D.
New York University (Bellevue Med. Ctr.)	Sidney Rubenfeld, M.D.
State Univ. of New York (Syracuse)	Paul A. Riemenschneider, M.D.
University of Alabama	William H. Riser, Jr., M.D.
University of Arkansas	I. Meschan, M.D.
University of Kansas	Galen M. Tice, M.D.
University of Louisville	Herbert D. Kerman, M.D.
Univ. of Mississippi	A. C. Guyton, M.D.
University of Nebraska	Howard B. Hunt, M.D.
University of Southern California	Henry L. Jaffe, M.D.
University of Tennessee	David S. Carroll, M.D.
University of Texas (Medical Branch, Galveston)	
University of Texas (M.D. Anderson Hospital)	Gilbert H. Fletcher, M.D.
University of Virginia	George Cooper, M.D.
Vanderbilt University	C. C. McClure, M.D.
Wake Forest College	J. Robert Andrews, M.D.
Wayne University	James E. Lofstrom, M.D.

APPENDIX IV

SPECIAL TRAINING DIVISION

I. Consultant to Special Training Division

Cyril L. Comar	University of Tennessee - AEC Ag. Research Program.

II. Lecturers Assisting in Training Program

Paul C. Aebersold	Atomic Energy Commission
Elda E. Anderson	Oak Ridge National Laboratory
R. Ballentine	McCollum-Pratt Institute
William E. Barbour, Jr.	Tracerlab, Inc.
D. Z. Beckler	Atomic Energy Commission
C. E. Birchenall	Princeton University
Oscar Bizzell	Atomic Energy Commission
Rita Bogoroch	Harvard School of Dental Medicine

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6/30/54

Eighth Annual Report

of the

Oak Ridge Institute of Nuclear Studies

June 30, 1954

Operating Under Contract

With the

UNITED STATES ATOMIC ENERGY COMMISSION

AEC, Oak Ridge, Tenn. 10-1-54-3,000-W-25969

Medical Division

THE Medical Division's role in cancer research is the evaluation of radioactive isotopes and radiations in therapy, with cular emphasis on work which can best be ed out at Oak Ridge because of its proximity Oak Ridge National Laboratory on the one hand, to medical schools on the other. This interiate role of the Division gives it an unusual tunity to carry out its work. A good example he benefits to be derived from this arrangement he progress made during the year in the telepy program. The Teletherapy Evaluation rd, a joint activity of the Division and 22 ical schools, saw its medium-curiage (hectoe) unit into service. In the meantime, the dioisotope Development Department of Oak dge National Laboratory concentrated a 1540-e source of radioactive cesium for use in the B's kilocurie unit, itself almost complete at s end.

The Division's principal activities may be ded into four areas as follows:

a. Basic studies of internally-administered opes.

b. Clinical studies of these isotopes.

c. The external use of isotopes in therapy, bly in multicurie radiation sources.

d. A training program providing facilities and ff to instruct medical residents, research partints, and others in the use of radioactive mals in medicine.

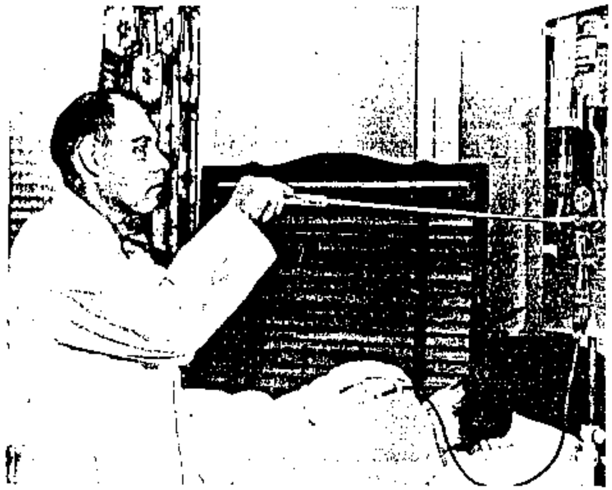
Each of these areas will be discussed in e detail.

SIC STUDIES OF INTERNALLY-DMINISTERED ISOTOPES

The problem of finding a suitable isotope for rnal use has many aspects. The radiation en off must have desirable characteristics. material must be nonpoisonous and should biologically inert (excluding, of course, the abolically active isotopes, such as iodine phosphorus). It must be gotten to the desired cation and it must remain there if the site is receive selective irradiation. The isotope must ve a short half life, but not too short. It must accompanied by sufficient stable carrier to ure even spread of the isotope over the desired a.

The isotopes that received most attention ring the year were three members of the rare rth family, yttrium, holmium, and leutecium; llium-67, which has been studied for several ears; and chromic phosphate, in the same catory.

All of these isotopes were used as colloids or in ionic solutions behaving like colloids.



Administering radioactive isotopes to a patient.

CHROMIC PHOSPHATE

Chromic phosphate containing phosphorus-32 was among the first of the radioactive preparations to be investigated for internal therapeutic application, although interest was reduced somewhat by the difficulty of getting uniform batches of material. This compound incorporates the desirable radiation characteristics of a metabolic isotope in a biologically inert material. Chromic phosphate is being tested rather extensively once again. Major interest in the Medical Division is in intracavitary and interstitial use in prostate carcinoma. Interpleural administration of different batches of chromic phosphate were tested in a series of rats and a few dogs. Although there was variation in the batches because of empirical mechanical steps in the manufacturing process, in each case more than 90 per cent of the compound remained in the cavity into which it was introduced. About half of the radioactivity that left the cavity was found in the liver and spleen. There was very high activity in the mediastinal tissues.

YTTRIUM-90

Yttrium-90, a frequently-occuring fission product (5.4 per cent of fission waste is Y-90), has been the subject of the greatest amount of study among the internally-administered isotopes during the year. Animal tests determined the amount of carrier desirable and demonstrated the preferred acidity of the solution. Distribution has been studied in a large number of animals grouped according to the route of administration. The routes include intrapleural, intraperitoneal, intramuscular, subcutaneous, intravenous, intratumoral, and intraglandular administration. Radiochemical assay and autoradiographic records of a wide variety of tissues have been made. All of the results indicate consistently that yttrium with carrier behaves as a colloid and is effectively immobilized in the injected area. In intracavitary and interstitial application, as much as 98 per cent of the administered dose remained immobilized for as long as two half lives of the isotope.

Intraperitoneal studies of the radioyttrium preparation in Erhlich ascites tumor mice are in progress. About half of the dose remains in the ascitic fluid and half deposits on the serosal surfaces, although retention in the cavity appears almost complete.

Also under investigation is the interstitial use of yttrium-90 in the prostate and parametrium. Preliminary investigations in cooperation with one of the Harvard group of residents indicate a high retention in the injected area and a spread into the pattern of surrounding lymph nodes. If additional investigation confirms this distribution pattern, this use is of obvious clinical interest. An additional study initiated in cooperation with one of the Memphis groups of research participants at the end of the year sought to determine the effect of a previously-injected body pool of yttrium on the distribution of carrier-free yttrium. The possible application relates to the effect of a dose or doses of stable yttrium before the use of tracer or therapeutic doses.

HOLMIUM AND LUTECIUM

These isotopes were studied to determine their intrinsic merits and to provide additional information on the rare earths as a whole. Both have desirable radiation characteristics for use. Lutecium-177 has a half life of 6.8 days and emits soft beta and gamma rays; holmium's 27-hour half life is long enough to be of clinical significance; it yields an energetic beta particle and one hard and one soft gamma ray. Stable holmium is 100 per cent abundant as holmium-165; by neutron capture pure holmium-166 may be obtained.

The possibility that the almost identical chemical behavior of lutecium and holmium (and perhaps other of the rare earths) produces a similar biochemical behavior is of much practical interest. If a similar behavior does characterize the series, a number of isotopes with desirable radiation characteristics may be selected from among the larger number of nuclides of the rare earths.

Another advantage is the possibility of using heterogeneous mixtures of rare earths as carriers for isotopes. Most of the rare earths are scarce and expensive in a highly purified state, although crude fractions of groups of rare earths are used in certain industrial and commercial commodities and are relatively inexpensive.

Could mixed fractions, or the more common rare earths, be used as carriers for the small amounts of pure elements needed for the radioactivity? At present, lutecium is scarce and expensive, with the cost of the stable element an appreciable part of the cost of the production of the nuclide. Observations using separately yttrium and lanthanum as carrier for lutecium-177 confirm this hypothesis; that is, it can be localized at the site of administration with either element added as carrier. In a few experiments the indication is the same for controlling the localization of holmium-166.

Work on the rare earth elements is continuing in the Division.

OTHER STUDIES

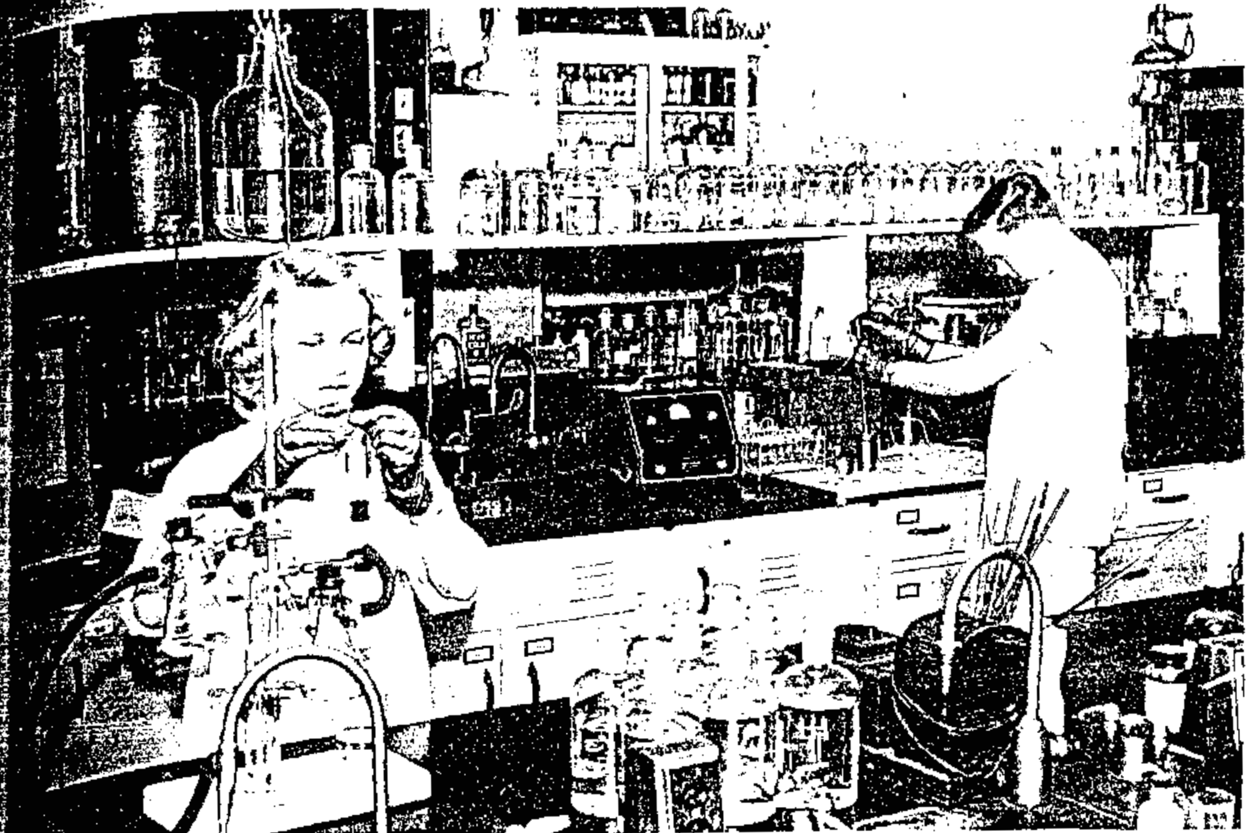
The Division is continuing the study of gallium-67, a cyclotron-produced isotope, as a possible therapeutic agent in the treatment of bone malignancies. It also has under study a number of other problems, either concerning the use of isotopes or the development of more refined techniques for counting and preparation of tissue samples.

A member of the Division staff has conducted a very interesting study of the postulate that radiorubidium is a biochemical substitute for radiopotassium and hence could be used to measure body potassium capacity. Radiocesium, another alkaline metal, also has been investigated as a potassium substitute.

Sulfur-35 has been used in two problems. One is the study of the use of sulfur in the formation of cartilage and its possible application. The other is a study of sulfur-labeled methionine in metabolism.

CLINICAL RESEARCH PROGRAM

Since human life is at stake in the clinical phase of the medical studies, the experimental work must of necessity be subordinated to the necessity for administering the best possible care to each patient. Consequently, more time and expense go into the care of the patient than into the study of the isotope. Although many patients receive a direct benefit from the use of various radioisotopes, complete success is seldom achieved. A detailed study of failures in treatment is therefore a necessary part of the program; this is of such importance that a portion of the



The biochemistry laboratory.

patients are accepted without hope of success. The final experiment in any drug problem must of necessity be carried out in the human being. When these studies are done with potentially lethal drugs such as radioisotopes, only terminal patients may be used. In such studies the only benefit the Division can offer the patient in repayment for his confidence is good nursing care and palliative treatment.

The intracaviatry use of colloidal radioisotopes has been a major clinical project in the Division for more than three years. Emphasis has been placed on the gathering of information on the metabolism, distribution, and histopathologic effects of isotope therapy. At the present time radioactive gold is still the principal therapeutic isotope in the Division, particularly in patients with a relatively favorable outlook in which the clinical staff hesitates to use an untried agent, such as yttrium-90 or Lu-177 or the chromium salt of phosphoric acid. Most patients in this group receive a tracer dose of yttrium-90 and a therapeutic dose of gold-198. The Division continues its vigorous follow-up observations on the pathologic effects of gold-198.

Radioactive chromic phosphate has been tried as a substitute for gold-198. Although it has good radiation characteristics and has a longer half life than gold, it appears to disassociate somewhat and a significant amount is excreted in the urine.

The Division is just beginning its clinical work on yttrium-90. Preliminary work indicates that it remains well localized, with negligible blood levels and excretion.

The Division has not pursued extensively the interstitial use of colloids because special surgical skills and technical equipment not now available to the Division are needed.

Gold-198 has been used intravenously for the treatment of certain cases of chronic granulocytic leukemia. It was found to be of little value as a form of therapy for some liver tumors.

Gallium-67 is being used to treat bone lesions, although it has been difficult to find patients in whom any satisfactory evaluation of effect could be made. Bone lesions are often chronic and X-rays may fail to show their progression or regression. Retention and local concentration is best in osteoblastic lesions. Bone marrow damage is the chief factor limiting use.

DIAGNOSTIC AND INVESTIGATIONAL USES

Concurrent with its therapeutic program, the Division has conducted an active diagnostic and

One of the Medical Division's basic animal research laboratories, located at the University of Tennessee-Atomic Energy Commission Agricultural Research Program.

investigational program, in part for its own use and as a part of its training program. Studies include:

1. External surveys of liver after gold-198 administration.
2. Rate of disappearance of tracer doses of gold from blood as an index of reticuloendothelial function.
3. Uptake of colloids by normal and pathologic leukocytes.
4. Metabolism of sulfur-labeled amino acids and inorganic sulfur.
5. Radioisotopes in relation to plasma protein fractions.
6. Red cell mass, plasma volume, red cell survival, and iron metabolism in malignant diseases.
7. Hematologic disorders and polycythemia.
8. The mechanisms of fluid collection in ascites.

INVESTIGATIONS USING IODINE-131

A continued study of carcinoma of the thyroid has been in progress since the first patient was accepted in the Medical Division hospital. As a part of this study, a special interest has developed in the use of radioiodine to destroy the normal thyroid gland. Histologic and autoradiographic observations have been made. A further outgrowth of this was a study in dogs to determine the effect of radiation from external sources upon the metabolism of tracer doses of iodine-131.

The Division also has studied blood levels of radioactivity and has conducted paper chromatographic analyses on metabolism iodine compounds. A few cases of hyperthyroidism have been admitted for treatment with iodine-131.

Other studies of clinical interest under way in the Division are of bone marrow morphology, including the radiation effects and the pattern of malignant invasion.

Some patients with polycythemia vera and leukemia are accepted for treatment with phosphorus-32, largely in connection with the training program.

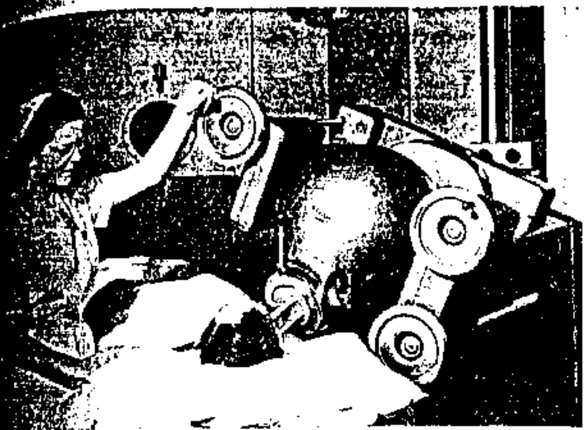
EXTERNAL USE OF ISOTOPES

Next to the care of patients, which is always an overriding consideration in the work of the Medical Division, the activity receiving the most attention during the year was the study carried out by the Division and the Teletherapy Evaluation Board of the external use of isotopes in therapy. Among the most important aspects of this program are:

1. The development of suitable mechanical devices to house the source and direct the radiation beam.
2. The provision of adequate shielding requirements in the treatment room.
3. The establishment of a general field of knowledge in dosimetry.
4. The development of suitable instrumentation and other devices to provide relatively simple operating controls.
5. A comparative study of the different isotopes that appear suitable for teletherapy devices.
6. The setting up of comprehensive clinical programs to evaluate the entire teletherapy program.
7. The standardization of design for radiation sources in order to increase their availability and reduce their cost.

The two major classes of teletherapy units now under investigation by the TEB are a cesium-137 moving-beam unit in the kilocurie range, and a cobalt-60 machine in the range of 300-600 curies (hectocurie unit).

An extensive clinical testing program is just

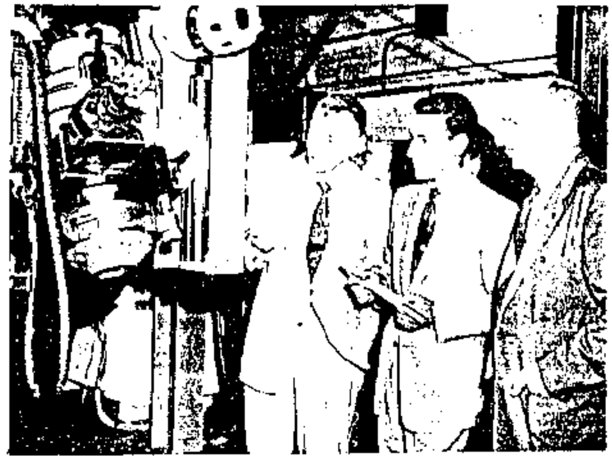


The hectocurie cobalt-60 unit using a simulated patient.

Beginning on the hectocurie cobalt-60 machine, which is designed for use by practicing radiologists. The first such unit was delivered to the Medical Division in August and seven members of the Teletherapy Board have already ordered units. About 75 per cent of the time of these units will be concerned with the medical schools' own research and clinical program, and about 25 per cent will be concerned with the joint clinical program of the TEB.

In contrast to this simple cobalt-60 unit is the rotational kilocurie unit which was nearing completion at year's end. This unit, costing in the neighborhood of $100,000, will permit the testing of 10,000-curie cesium sources when they become available, as well as lesser sources of cobalt and europium, other isotopes that have characteristics suitable for teletherapy units. A great variety of movements has been incorporated into the machine. Using this unit, the TEB should be able to test the efficacy of the three isotopes, the value of rotational therapy, and the best treatment distances. Used in dosimetry studies, the unit would provide much information not now available. A novel feature of the machine is a built-in computing device that will direct a pre-set treatment pattern. Such a device probably will be incorporated in so-called "practical" teletherapy machines to save time for the radiologist and thus reduce the cost of treatment. At the other end of the scale, a study is well underway of the use of low curiage units.

As part of the external therapy program, the Medical Division is studying the absorption of gamma rays from cobalt, cesium, europium, gold, iodine, and several other isotopes. The study involves attenuation measurements in four kinds of materials: elements and simple salts of elements, tissue-like materials of known composition, human tissue, and building and shielding materials. Studies are almost complete for gold



New cancer teletherapy unit built by W. F. and John Barnes Company, Rockford, Illinois, for use of radioactive cesium is examined by Marshall Brucer, M.D., Chairman of the Medical Division, and Teletherapy Evaluation Board members Kenneth Loeffler, M.D., (Jefferson Davis Hospital, Houston) and Vincent Collins, M.D. (Baylor University School of Medicine).

and cesium and are nearing completion for cobalt.

Shielding tests include studies of wall-type shielding for large areas, narrow beam shielding, spherical broad beam close-in shielding with air scatter and true broad-beam conditions with scatter inside the shielding material.

Dosimetry investigations involve studies of the effect of the size of the source, shape, the energy, and the number of sources. These are to be determined in regular geometric phantoms, human volume phantom, simulated plastic human phantom, simulated human organs, and excised animal organs.

Instruments and equipment available for these studies include an automatic isodose plotter, a series of "standard man" phantoms, and a range of ionization measurement devices to simulate many human therapy dosimetry conditions.

In connection with the development of standard radiation sources, the Division with the Isotopes Division of AEC and Atomic Energy of Canada, Limited, sponsored a series of industrial conferences on teletherapy. Representatives of all manufacturers of X-ray equipment, representatives of the national laboratories, and other interested individuals were invited to attend. The groundwork was laid at these conferences for important standardization work in radiation sources.

TRAINING PROGRAM

A part of the responsibilities of the Medical Division is the provision of facilities for training medical personnel in radioisotopic techniques developed in Oak Ridge. The major activity during the year in this respect was the offering in September, in cooperation with the Special Training Division, of a two-week course in late developments in the field of isotopic medicine. Many of the nation's outstanding figures in the use of radioisotopes in medicine participated in the course, which was attended by about 122 persons. Lectures given in the course will be published by the Government Printing Office early in 1955.

During the year, 7 residents from medical schools served with the Division. A total of 4 research participants from universities were engaged in research at the Division. A large number of consultations were held with visiting personnel from medical schools in medical practice.

This program is a two-way affair. It enables members of the Division staff to keep acquainted with late developments in the medical schools and universities. The individual interests of residents or research participants have led to many of the Division's most engaging research activities.

PUBLICATIONS FROM THE MEDICAL DIVISION (FISCAL YEAR 1954)

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HAFNIUM COMPLEXES FOR BIOLOGICAL INVESTIGATION. E. Macdonald, and C. T. Bahner. *Proceedings of the Society for Experimental Biology and Medicine*, Vol. 83, 1953, pages 801-804.

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TELETHERAPY DESIGN PROBLEMS. M. Brucer. *Radiology*, Vol. 62, No. 1, January 1954, pages 91-98.

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PATHOLOGIC CHANGES IN NORMAL HUMAN THYROID TISSUE FOLLOWING LARGE DOSES OF I 131. G. A. Andrews, R. M. Kniseley, R. R. Bigelow, S. W. Root, and M. Brucer. *American Journal of Medicine*, Vol. 16, No. 3, March 1954, pages 372-381.

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EFFECT OF CHAMBER VOLTAGE ON ELECTRON BUILD-UP MEASUREMENTS. J. E. Richardson. *Radiology*, Vol. 62, No. 4, April 1954, pages 584-588.

BIOCHEMICAL CONSIDERATIONS OF DISTRIBUTION. G. C. Kyker. *American Journal of Medical Sciences*, Vol. 227, No. 5, May 1954, pages 572-589.

A STANDARD COBALT 60 TELETHERAPY SOURCE CAPSULE. M. Brucer. *Nucleonics*, Vol. 12, No. 6, June 1954.

LIST OF PUBLICATIONS IN PRESS

SKIN DOSE FROM A COBALT 60 TELETHERAPY UNIT. J. E. Richardson, H. D. Kerman, and M. Brucer. *Radiology*.

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ABDOMINAL CARCINOMATOSIS AND PORTAL CIRRHOSIS: THE RATES OF INTERCHANGE BETWEEN THE VASCULAR COMPARTMENT AND PERITONEAL CAVITY. M. P. Tyor. *Journal Laboratory and Clinical Medicine.*

LOCALIZATION ON ANTIMONY IN BLOOD. C. T. Bahner. *Proceedings of the Society for Experimental Biology and Medicine.*

ACCEPTED FOR PUBLICATION

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THE DISTRIBUTION OF INTERSTITIAL AND INTRACAVITARY INJECTIONS OF CERTAIN RADIOCHEMICAL PREPARATIONS OF MEDICAL INTEREST. G. C. Kyker. *Bulletin of the Medical Association of Puerto Rico.*

SUBMITTED FOR PUBLICATION

A STANDARD COBALT 60 TELETHERAPY SOURCE CAPSULE. M. Brucer. *Canadian Journal of Radiology, Strahlentherapie, and Acta Radiologica.*

MEETINGS AND PROFESSIONAL VISITORS AT THE MEDICAL DIVISION

	Meetings	Visitors
July	0	20
August	6	20
September	6	9
October	5	15
November	2	9
December	2	6
January	5	5
February	7	16
March	7	13
April	3	18
May	2	10
June	2	9
Total	47	120

ORINS HOSPITAL PATIENT CENSUS

Admitted to the ORINS Hospital during the fiscal year were 97 new patients from the following states:

Tennessee	47 (plus 22 out patients)
Virginia	9
South Carolina	4
Florida	11
North Carolina	12
Kentucky	2
Louisiana	1
Puerto Rico	1
Georgia	4
Alabama	4
Ohio	1
Texas	1
Total	97 (plus 22 out patients)

Total patient days during each month of the fiscal year are as follows:

July	536
August	566
September	350
October	404
November	398
December	347
January	339
February	371
March	374
April	461
May	488
June	377
Total Patient Days	5,011

ISOTOPES USED BY THE MEDICAL DIVISION

	Millicuries
Antimony-121, 124	225
Calcium-45	7
Cesium-134	10
Chromium-51	8
Europium-152, 154	1.50
Gallium-67	2587.4
Gold-198	8275
Holmium-166	64.3
Iodine-131	1350
Iron-59	3.65
Lutecium-177	192
Phosphorus-32	472

Potassium-42	390		2 shipments not yet assayed
Rubidium-86	145		
Sodium-24	12		
Sulfur-35	2		
Yttrium-90	82.6	plus	450 curie source for hectocurie tele-therapy machine
Yttrium-91	40		
Cobalt-60	275 Milligrams (estimated)		

APPENDIX I

PERSONNEL OF THE OAK RIDGE INSTITUTE OF NUCLEAR STUDIES

(as of July 1, 1954)

Council

David H. Morgan	A & M College cf Texas
William Vann Parker	Alabama Polytechnic Institute
Karl F. Herzfeld	Catholic University of America
H. L. Hunter	Clemson Agricultural College
W. M. Nielsen	Duke University
Howard M. Phillips	Emory University
[illegible] W. Carothers	Florida State University
R. L. Sweigert	Georgia Institute of Technology
Richard C. Keen	Louisiana State University
[illegible] P. Etheredge	Mississippi State College
*C. G. Brennecke	North Carolina State College
T. W. Bonner	Rice Institute
Wayne Rudmose	Southern Methodist University
Robert T. Nieset	Tulane University
R. W. Brown	Tuskegee Institute
Marten ten Hoor	University of Aiabama
R. R. Edwards	University of Arkansas
Roland B. Eutsler	University of Florida
George H. Boyd	University of Georgia
Lyle R. Dawson	University of Kentucky
R. C. Ernst	University of Louisville
Ronald Bamford	University of Maryland
Fred W. Kellogg	University of Mississippi
C. D. Van Cleave	University of North Carolina
Simon Wender	University of Oklahoma
Facundo Bueso	University of Puerto Rico
H. W. Davis	University of South Carolina
E. A. Waters	University of Tennessee
Malcolm Y. Colby	University of Texas
John H. Yoe	University of Virginia
R. T. Lagemann	Vanderbilt University
Frank C. Vilbrandt	Virginia Polytechnic Institute

Board of Directors

Paul Magnus Gross, *President*
Vice President, Duke University

Clifford Keith Beck, *Vice President*
Professor and Head of the Department of Physics, North Carolina State College

Jesse Wakefield Beams, *Director*
Professor of Physics, University of Virginia

George Hugh Boyd, *Director & Chairman of the Council*
Dean of the Graduate School, University of Georgia

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Dean of Engineering, Columbia University

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President, Rice Institute

Warren Charles Johnson, *Director*
Professor and Chairman of the Department of Chemistry, University of Chicago

Clarence Edward Larson, *Director*
Director, Oak Ridge National Laboratory

Hayden Coler Nicholson, *Director*
Dean of the School of Medicine, University of Arkansas

Louis Arthur Pardue, *Director*
Vice President, Virginia Polytechnic Institute

Merlin Dewey Peterson, *Director*
Professor and Head of the Department of Chemistry, Vanderbilt University

II. Personnel

OFFICE OF THE EXECUTIVE DIRECTOR

William G. Pollard, Executive Director

George B. Pegram, Consultant

Anna Mae Anderson	Secretary
Jane Ethridge	Record Clerk
Martha L. Fletcher	Record Clerk
Marion Garber	Librarian
Rubye Ison	Record Clerk
Dixon Johnson	Hd., Info. Dept.
Helen Lewis	Secretary, Senior
Louise Markel	Librarian
Loyce McIlhenny	Info. Asst.
J. W. Mumford	Assistant Treasurer
Paul E. Pearson	Auditor
Reinhold Schlueter	Library Supv.
Dorothy A. Wells	Clerk-Typist

*Died August 2, 1954

1026690

OFFICE OF ADMINISTRATION

Paul M. Elza, Manager of Administration

William Blankenship	Maint. Mech. I
George N. Brent	Inst. Engineer
Ralph B. Briggs	Maint. Mech. II
Cecil H. Brown	Maint. Mech. II (temp.)
John M. Burns	Helper (temp.)
William C. Busby	Management Asst.
Joan R. Clouse	Stenographer
Barbara Cole	Stenographer
Paul G. Davis	Storekeeper
Charles H. Day	Stockkeeper
W. G. Disney	Personnel Asst.
Harrison E. Elliott	Purchasing Agent
Ellen Epperson	Accountant
Dewey Ferguson	Maint. Mech. I
Opal C. Flinchem	Secretary
Elizabeth M. Goodin	Clerk-Typist
Walter Graves	Instrument Mech.
Mary Ann Groeniger	Clerk-Typist (temp.)
Barbara Guinn	Clerk-Typist
Johnnie Harvest	Custodian
Nathaniel Hill	Inst. Engineer
Joseph Houston	Photographer
Faye J. Jones	Record Clerk
Harry E. Kimble	Sr. Instrument Maker
Arch E. Long	Instrument Mech.. Electronic
Kaye Margrave	Record Clerk
T. W. Martin	Hd., Tech. Serv. Dept.
Barbara McClannahan	Section Supervisor
Margaret Ann McKinney	Accounting Clerk
Dozier E. McKinnon	Helper
Dorothy Nanney	Accounting Asst.
Arville R. Nelson	Maint. Mech. I
Clyde Parton	Helper (temp.)
William Perry	Mail Clerk
Kathleen J. Reuter	Stenographer
William Rhodey	Maint. Mech. II
J. W. Rose	Hd., Fiscal Serv. Dept.
H. J. Russell	Maint. Mech. I
Mary E. Russell	Section Supervisor
Wendell H. Russell	Hd., Manag. Serv. Dept.
Carl J. Rutherford	Accountant
W. D. Schwartzman	Property & Supply Asst.
Amon D. Silcox	Maint. Mech. I (temp.)
Lois E. Smith	Clerk-Typist
Rosella Stooksbury	Receptionist
Robert Taylor	Delivery Man
Marvin Triplett	Section Supervisor
Johnny Vaughn	Helper
Leonard Vickery	Helper
Decatur M. Walker	Inst. Maker (temp.)
Charles Wallace	Cabinet Maker
John H. Wells, Jr.	Maint. Mech. I (temp.)
James Wilde	Inst. Engineer
Herbert V. Wilkins	Procedures Asst. (temp.)
James W. Wright	Maint. Mech. I (temp.)

UNIVERSITY RELATIONS DIVISION

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Nelle Strange	Fellowship Asst.
Mary Lou Whitten	Clerk-Typist
Alma Ann Williams	Secretary

MEDICAL DIVISION

Marshall Brucer, Chairman

Lucy M. Amburn	Nurses Aide
Ugo Amelio	Lab. Asst.
Elizabeth B. Anderson	Research Assoc.
Gould A. Andrews	Chief, Clin. Services
Edward T. Arakawa	Research Assoc.
Rufus Bolton	Custodian
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Faye E. Chance	Lab. Tech.
Roberta B. Clouser	Staff Nurse
Betty M. Cooper	Sr. Scientist
Henry P. Copeland	Research Asst.
Mary N. Craig	Staff Nurse
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Lewis Dobson	Helper
Timothy Dowdell	Helper
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James Eldridge	Research Assoc.
William C. Fields	Lab. Tech.
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Patricia Fisher	Nurse-Gen. Duty
Eula B. Hopper	Stenographer
Peggy C. Free	Nurse-Gen. Duty
William D. Gibbs	Research Tech.
Joe Gray	Research Assoc.
Elizabeth Grindstaff	Nurses Aide
J. H. Harmon	Admin. Officer
Raymond L. Hayes	Scientist
Eva Hodgens	Research Asst.
George R. Holloway	Orderly
Mabel Hurst	Med. Records Librarian
Elmer L. Keller	Research Tech.
Ralph M. Kniseley	Prin. Scientist
Granvil Kyker	Prin. Scientist
Vivian D. Lay	Record Clerk
Dail W. Longaker	Lab. Asst. (temp.)
William C. Martin	Lab. Tech.
Barbara J. McCarroll	Nurse-Gen. Duty
James W. McGill	Lab. Aide
Ida L. Meadows	Nurse-Gen. Duty
Margie R. Meeks	Receptionist
Suzanne B. Nicholson	Clerk-Typist (temp.)
*Priscilla A. Oliver	Occup. Therapist

*Part-time employees

...a Pack	Nurses Aide
...s Palmer	Asst. Clinician
...tie Bell Perry	Custodian
...omi D. Presnell	Nurse-Gen. Duty
...J. Rafter	Research Tech.
...nche Richardson	Record Clerk
...h V. Robison	Nurse-Gen. Duty
...muel Root	Clinician
...Irwin Roth	Lab. Tech. (temp.)
...llie P. Simmons	Custodian
...son Stephens	Lab. Tech. (temp.)
...tha G. Stewart	Research Tech.
...illy L. Stump	Research Tech.
...ry Sutliff	Nurse-Supv.
Elizabeth L. Thomas	Lab. Tech.
William Walker	Custodian
Elmer L. Warren	Research Tech.
Verda L. Wells	Nurse-Gen. Duty
Pearl E. Wyrick	Clerk-Typist

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Billy Joe Pitts	Custodian
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Margaret L. Scott	Clerk-Typist
Donald R. Smith	Sr. Scientist
Ardell C. Stewart	Lab. Tech.
Edith Wilson	Secretary

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Sabelia J. Atkins	Receptionist
*Jane Blankenship	Helper
Ann J. Caldwell	Receptionist (temp.)
*Charles S. Davis	Museum Aide
June N. Davis	Secretary
*Robert E. Deweese	Helper
W. Earl Duff	Admin. Asst.
Wheeler Fain	Custodian
John N. Fox	Exhibits Mgr.
Renfro Henderson	Custodian
Jack D. Johnson	Exhibits Mgr.
Dewey E. Large	Management Asst.
Robert R. McDonald	Maint. Mech. I
*Jacques R. Nitschke	Museum Aide
George B. Presley	Display Artist
*Harold E. Price	Display Artist (temp.)
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Theodore Robbins	Maint. Mech. I
Robert C. Rothermel	Museum Asst.
*Crawford Sachs	Helper
Larry H. Sharp	Exhibits Designer
Carolyn S. Miller	Receptionist
Robert M. Summers	Museum Aide
Robert G. Wells	Museum Aide
*Peggy Ann Williams	Helper

Science Fair

Dewey Large	Field Representative

TERMINATIONS

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Kathleen V. Denis	Secretary
Martha H. Williams	Record Clerk

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John M. Burns	Helper (temp.)
Daniel W. Capps	Procedures Asst. (temp.)
Victor A. Cook	Maint. Mech. I (temp.)
John H. Fenton	Hd., Mgt. Serv. Dept.
Virginia M. Gilpatrick	Vari-Typist
Billie Jean Hurt	Clerk-Typist (temp.)
Carl E. Johnson	Maint. Mech. I
Jenny M. Rose	Clerk-Typist
Gloria J. Roseberry	Vari-Typist
Nancy V. Russ	Record Clerk
*William L. Scott, Jr.	Mechanical Engineer
Ruth C. Shular	Clerk-Typist
Hugh K. Simpson	Custodian
Mavis V. Uthe	Record Clerk
R. Kenneth Youngblood	Maint. Mech. II

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Frances A. Crowley	Stenographer
William Dryden	Administrative Asst.
Trula V. Hobbs	Secretary
Russell S. Poor	Chairman, Univ. Rel. Div.

MEDICAL DIVISION

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Gladys E. Cooper	Nurse-Gen. Duty
John W. Deathriadge	Custodian
Bobbie J. Giovannucci	Nurse-Gen. Duty
Betty C. Gray	Lab. Tech.
Geneva Hefner	Nurses Aide
Mary S. Hyder	Nurse-Gen. Duty
Edith K. Kees	Nurses Aide
Mary M. Knight	Lab. Tech.
Clara J. Leslie	Nurse-Gen. Duty
Evan D. McKissic, Jr.	Custodian
John C. Rowland	Custodian
Elsie P. Ruggles	Nurse-Gen. Duty
E. Melvin Russ	Lab. Tech.
*Marie Scharl	Nurses Aide
*Mary P. Smyser	Lab. Tech.
Barbara H. Stevens	Nurse-Gen. Duty
Malcolm P. Tyor	Clinician
Margaret Watson	Nurse-Gen. Duty
James O. White	Orderly

*Part-time employees

SPECIAL TRAINING DIVISION

Iziah Jones	Custodian
Myron S. McCay	Instructor (temp.)
Frances S. Neal	Secretary
Walter B. Poe	Custodian (temp.)

EXHIBITS DIVISION

Mary S. Bowman	Helper (temp.)
Curtis Coley	Maint. Mech. I
David L. DeJamette	Chmn., Exhibits Div.
Willie H. Dunn	Maint. Mech. I
Jean E. Fahey	Receptionist
Clarence Hensley	Maint. Mech. I
Alice N. Montgomery	Stenographer
Donald G. Robertson	Museum Asst.
Mary S. Tuccinardi	Secretary

Aaron Ganz	University of Tennessee Memphis, Tennessee
Robert A. Woodbury	University of Tennessee Memphis, Tennessee
L. D. MacDonald	University of Mississippi University, Mississippi

IV. Residents

Physicians

Albert G. Lewis, Jr.	University of Alabama Birmingham, Alabama
Erich Goldmeier	Beth Israel Hospital Boston, Massachusetts
Julio Toriello	Massachusetts General Hospital Boston, Massachusetts
William C. Moloney	Duke University Durham, North Carolina

Air Force Physician

Capt. Norman O. Harris	School of Aviation Medicine Randolph Field, Texas

Physicist

Jack Trombka	Wayne University Detroit, Michigan

Pharmacologist

Ernest A. Daigneault	University of Tennessee Memphis, Tennessee

V. Post-Resident Staff Members

A. S. MacMillan, Jr.	Massachusetts General Hospital Boston, Massachusetts
Paul M. St. Aubin	Massachusetts General Hospital Boston, Massachusetts

VI. Fellows

Fulbright Fellow

H. T. Oddie	University of Arkansas Little Rock, Arkansas

Damon Runyon Memorial Fund for Cancer Research Fellow

Chiyeko Okawa	St. Luke's International Hospital Tokyo, Japan

VII. Short-term Medical Student

Dail W. Longaker	University of Virginia Charlottesville, Virginia

VIII. Teletherapy Evaluation Board

Institution	Representative on TEB
Baylor University	Vincent Collins, M.D.
Creighton University	James F. Kelly, Jr., M.D.
Duke University	Robert J. Reeves, M.D.
Emory University	H. Stephen Weens, M.D.
Louisiana State Univ.	Walter J. Burdette, M.D.
Medical College of Virginia	Frederick B. Mandeville, M.D.
New York University (Bellevue Med. Ctr.)	Sidney Rubenfeld, M.D.
State Univ. of New York (Syracuse)	Paul A. Riemenschneider, M.D.
University of Alabama	William H. Riser, Jr., M.D.
University of Arkansas	I. Meschan, M.D.
University of Kansas	Galen M. Tice, M.D.
University of Louisville	Herbert D. Kerman, M.D.
Univ. of Mississippi	A. C. Guyton, M.D.
University of Nebraska	Howard B. Hunt, M.D.
University of Southern California	Henry L. Jaffe, M.D.
University of Tennessee	David S. Carroll, M.D.
University of Texas (Medical Branch, Galveston)	Robert N. Cooley, M.D.
University of Texas (M.D. Anderson Hospital)	Gilbert H. Fletcher, M.D.
University of Virginia	George Cooper, M.D.
Vanderbilt University	C. C. McClure, M.D.
Wake Forest College	J. Robert Andrews, M.D.
Wayne University	James E. Lofstrom, M.D.

Committees of the Teletherapy Evaluation Board

Executive Committee (elected by the TEB)

To serve 1 year:

Herbert D. Kerman, M.D.	University of Louisville
C. C. McClure, M.D.	Vanderbilt University
Marshall Brucer, M.D.	Medical Division, Oak Ridge Institute of Nuclear Studies

To serve 2 years:

Vincent Collins, M.D.	Baylor University
Henry L. Jaffe, M.D.	University of Southern California
James E. Lofstrom, M.D.	Wayne University
Carl E. Nurnberger	University of Tennessee

Subcommittees (appointed by the Executive Committee)

No. 1. Source Evaluation and Shield Design

Herbert D. Kerman, M.D.	University of Louisville
David S. Carroll, M.D.	University of Tennessee
Carl E. Nurnberger	University of Tennessee
John Tolan	Emory University

No 2. Small Source Design

Henry L. Jaffe, M.D.	University of Southern California
John Isherwood	Brooke Army Medical Center, Fort Sam Houston
James F. Kelly, Jr., M.D.	Creighton University
H. Stephen Weens, M.D.	Emory University
Harold W. Lewis, M.D.	Duke University

No. 3. Rotational Methods

Kenneth Loeffler	Jefferson Davis Hospital, Houston
J. Robert Andrews, M.D.	Bowman Gray School of Medicine
Frederick B. Mandeville, M.D.	Medical College of Virginia
C. C. McClure, M.D.	Vanderbilt University

No. 4. Housing Design

...es E. Lofstrom, M.D.	Wayne University
...l A. Riemenschneider, M.D.	State University of New York (Syracuse)
...ert J. Reeves, M.D.	Duke University
...ney Rubenfeld, M.D.	New York University (Bellevue Medical Center)

No. 5. Clinical Program

...cent Collins, M.D.	Baylor University
...dore Meschan, M.D.	University of Arkansas
...orge Cooper, M.D.	University of Virginia
Galen M. Tice, M.D.	University of Kansas
Herbert D. Kerman, M.D.	University of Louisville

No. 6. Clinical Physicist Training Program

Frank Hoecker	University of Kansas
Walter J. Burdette, M.D.	Louisiana State University
William H. Riser, M.D.	University of Alabama
Howard B. Hunt, M.D.	University of Nebraska
Arthur C. Guyton, M.D.	University of Mississippi

Marshall Brucer, M.D., ORINS Medical Division, Chairman of the TEB, is a member *ex officio* of all subcommittees.

APPENDIX III

MEDICAL DIVISION

I. Medical Advisory Panel

George T. Harrell, Chairman
University of Florida College of Medicine

R. Lee Clark	M. D. Anderson Hospital
Vincent P. Collins	Baylor University
Manuel Garcia	Tulane University of La.
Chalmers L. Gemmill	University of Virginia
Hayden C. Nicholson	University of Arkansas
Douglas H. Sprunt	University of Tennessee

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Ninth Annual Report

of the

Oak Ridge Institute of Nuclear Studies

June 30, 1955

Operating Under Contract
With the
UNITED STATES ATOMIC ENERGY COMMISSION

AEC, Oak Ridge, Tenn. 10-3-55-INS-19

Medical Division

THE Medical Division's over-all program of basic and clinical medical studies with emphasis on cancer and associated diseases and on the evaluation of the uses of radioisotopes and radiation in therapy continued this year with unabated vigor.

Because of space limitations, this report emphasizes the work of visiting personnel rather than the long-term projects of the permanent staff, whose work is presented in more detail in the ORINS semiannual progress report.

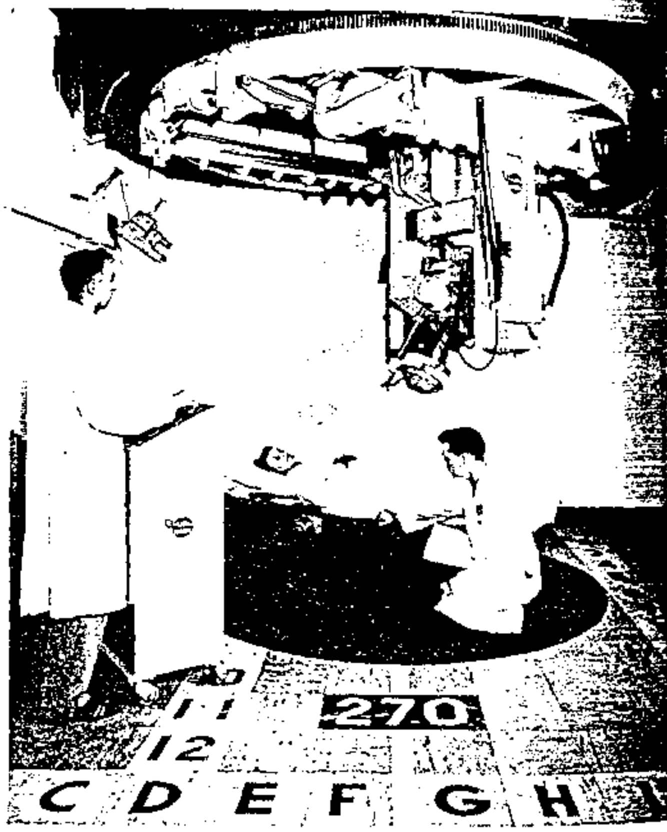
A milestone of progress was the installation in the Division of the Teletherapy Evaluation Program's kilocurie cesium-137 teletherapy machine. (The TEP is a joint activity of the Division and 22 medical schools.) This device permits irradiation of a specified area of diseased tissue with less harm to healthy tissue, through the use of a rotating beam.

A great aid to efficient handling of the Division's rapidly expanding out-patient service was the addition of a 3730-square-foot wing to the existing hospital building. The new wing provides a cobalt-teletherapy room; an out-patient waiting and patient day room; additional patient space to free some of the old patient area for laboratory needs; four small rooms to be used as examining rooms and offices; and a teletherapy mold and cast room; with one corner partitioned to house X-ray or europium equipment. A second addition, to permit establishment of an adequate laboratory-training facility for physicians, is planned.

The Medical Division's training program was more active than in any previous year. (See Appendix III for residents, research participants, and temporary staff members.) Division members participated to an increasing degree in the basic and special courses conducted at the ORINS Special Training Division, and aided in the presentation of these courses.

Editing was completed and publication begun on the proceedings of the second two-week advanced course in the techniques of using radioisotopes in medicine, held at the Institute in September of 1953.

During late spring and early summer a considerable amount of time was devoted to the preparation of lantern slides and special exhibits to be sent to the United Nations Conference on the Peaceful Uses of Atomic Energy in Geneva in August 1955.



The Teletherapy Evaluation Program's teletherapy machine utilizing a cesium-137 radiation source. Recently installed in the new wing of the Medical Division hospital, the device permits the focusing of a radiation beam on diseased tissue from any point in a hemispherical locus.

TELETHERAPY

Installation and preliminary testing of the TEP's 1540-curie, cesium-137 teletherapy unit is complete, and the close of the year saw the Division staff setting up the automatic isodose plotter. One useful research project has al-

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ready been carried out with the cesium unit. A research team from the University of Michigan brought a side of pork to Oak Ridge in March to run dosimetry studies with cesium radiation as part of an investigation of the applicability of fission products to food sterilization, especially in control of trichina.

Dosimetry studies have continued with the cobalt-60 teletherapy unit, which was also used for very limited therapy. A preliminary set of isodose curves for the cobalt-60 unit has been prepared, and at the year's end, was in press.*

Dosage Studies

The study of integral (total-body) dose from internally and externally applied radiation constitutes a major program of the Division. A two-compartment phantom, which simulates the human body, was constructed to contain a spherical tumor mass, and an integral-dose study was completed with chemical dosimetry. Integral dose was considered as a function of the distance from the source to the tumor, as a function of the size of the torso, and as a function of the position of the tumor in the torso, during both vertical-rotational and stationary treatment. Data from this study have been analyzed and an empirical formula has been derived for calculation under various conditions of the dose rate to the tumor and the integral dose.

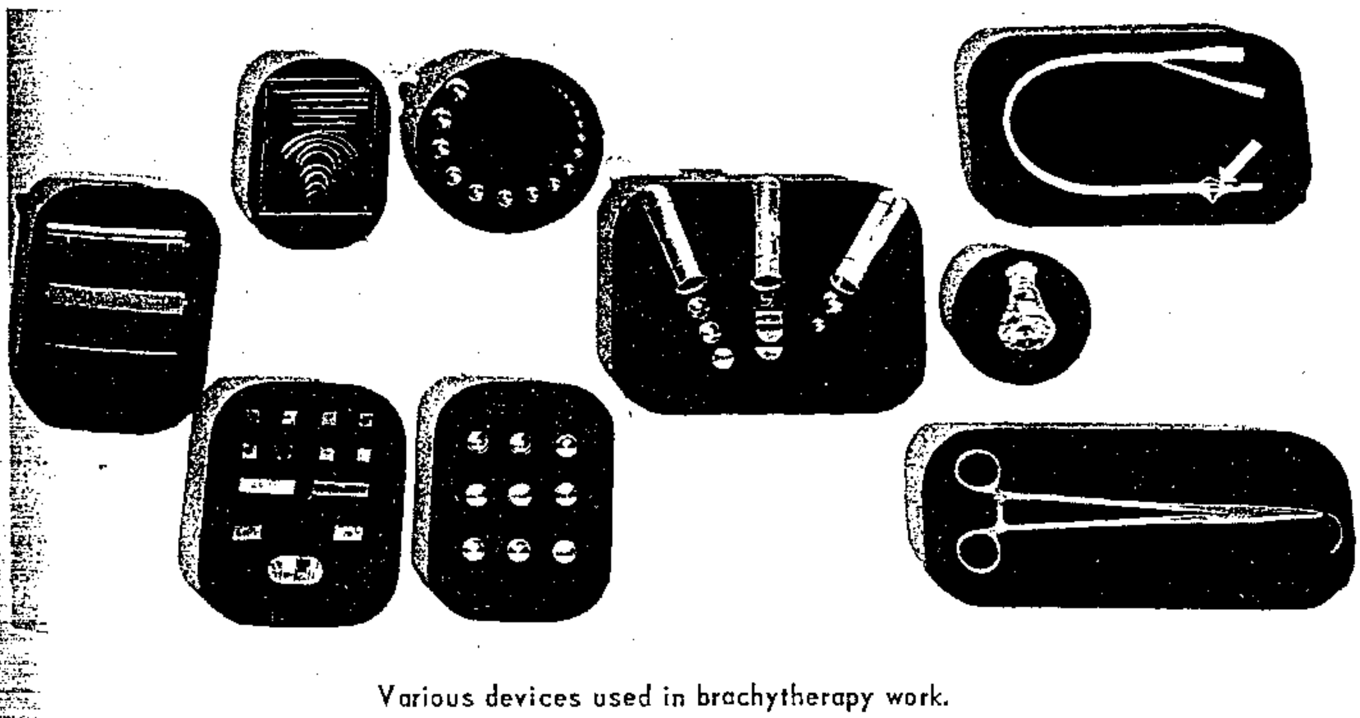
An extension of the studies of methods of chemical dosimetry has been conducted by Marion T. Clark of Emory University, an Oak Ridge summer research participant. Dr. Clark has worked on the synthesis of several phenyl-substituted 4-aminoantipyrines as potential reagents for the colorimetric determination of hydroxy benzoic acids producted by irradiation.

Dosage studies were carried out with the Teletherapy Evaluation Program's prototype hectocurie cobalt-60 unit. Future research will be undertaken using sources of 250-kvp X rays and cesium-137 for comparison; studies will also be made of the more intricate rotational patterns available with the Institute's new cesium-137 machine.

BRACHYTHERAPY

Many groups throughout the country are cooperating with the Medical Division in the investigation of various types of brachytherapy (close source-to-tissue distance) devices. At

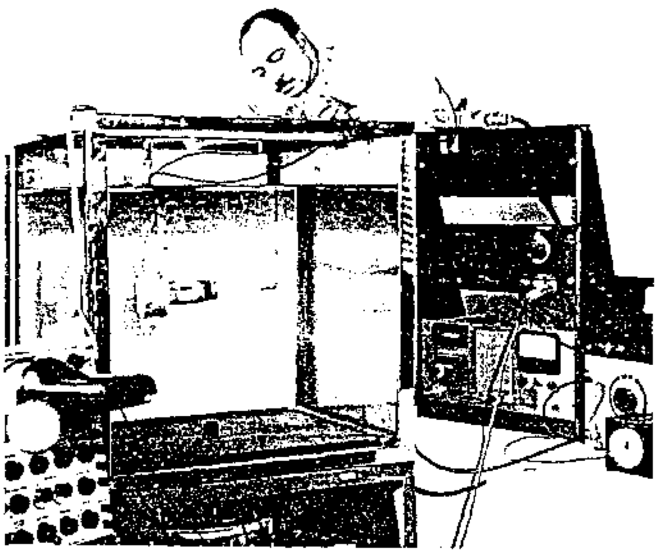
*"Isodose Charts for the Cobalt-60, Hectocurie Teletherapy Machine." ORINS-10. In press.



Various devices used in brachytherapy work.

the close of the year, plans were being made ˜or a July meeting of physicians experienced ‥n the design and use of brachytherapy devices; special attention was to be given to the development of a cobalt alloy, INCORAY, which virtually eliminates corrosion of the capsule material containing radiocobalt, and the resulting electron contamination.*

Kamal Mahmoud, an Egyptian physicist, spent three months at the Medical Division working with the problems of electron contamination around brachytherapy units.

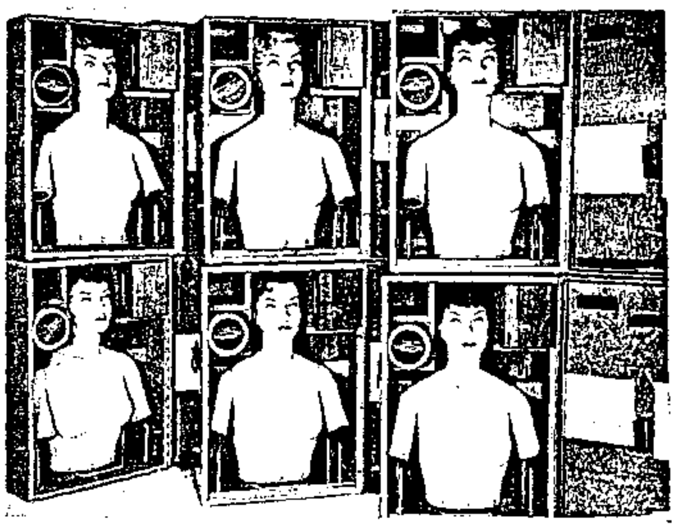


ˊamal Mahmoud, an Egyptian physicist who spent ;everal months of this year at the Medical Division, tudies electron contamination in brachytherapy evices.

ƆDINE-UPTAKE CALIBRATION

The Medical Division has undertaken the oordination of a new study (which is being conucted in cooperation with scientists at leadıg United States research institutions) of the ıethods of measuring the amount of radioiodine ɔsorbed by the human thyroid gland. In the ıst, methods and results of iodine-uptake calılations have been extremely variable; this informal survey will permit each participating scientist to measure the iodine-uptake in seven different "patients." These patients are seven half-body mannequins with simulated thyroids containing "mock-iodine" — a mixture of radioactive barium and cesium having radiation characteristics similar to those of iodine-131 and possessing the further advantage of having a useful life of more than ten years. The mannequins, loaded with variously radioactive thyroids, have been shipped to scientists at six institutions; other scientists in the same localities are also being invited to make similar uptake measurements. When the experiment is completed, in about a year, between 300 and 400 test results will be available for comparison, and standardization of techniques can be discussed more exactly. In addition, the Veterans Administration will conduct surveys in many of its hospitals, and the National Bureau of Standards will cooperate in calibration.

Scientists cooperating in this study are Benedict Cassen, University of California at Los Angeles; Raymond L. Libby, Los Angeles Veterans Administration Hospital; A. Stone Freedberg, MD, Harvard University Medical



Half-body mannequins used in the iodine-uptake survey being coordinated by the Medical Division are shown above in their traveling cases. Each kit contains, in addition to the mannequin, a mock thyroid gland, a set of "total-dose" (100 per cent) standards, a calibration kit, and a thigh section for an estimate of body background.

*Developed through the cooperation of E. M. Wise d research department of the International Nickel mpany; considerable work on manufactured products Larry Burnam of Baker Company.

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School; Robert T. Nieset, Tulane University; Edgar S. Gordon, MD, University of Wisconsin; Samuel Root, MD, Jacksonville, Florida; S. Allan Lough, Francis Delafield Hospital; T. H. Oddie, Bowman Gray School of Medicine (formerly a member of the University of Arkansas staff); and Herbert D. Kerman, MD, University of Louisville School of Medicine.

P. R. Bell, J. E. Francis, Jr., and C. C. Harris of Oak Ridge National Laboratory and Douglas A. Ross, MD, an Oak Ridge research participant from the University of Tennessee Medical School in Memphis, are collaborating with Division staff members on a new approach to the problem of instrumentation for thyroid-uptake and thyroid-counting problems, using the medical spectrometer, various types of flat-field probes, and focusing collimators; construction and evaluation of these instruments was in progress at the close of the year.

BASIC STUDIES

Interstitial and distribution and blood-clearance studies were especially emphasized in the Division's basic animal studies this year.

Biochemical research with yttrium-90 and lutecium-177, using ion-exchange columns and continuous paper electrophoresis, has yielded data on the reactions of rare earths in living systems. The increasing biochemical and medical interest in rare-earth elements (largely the result of studies with their isotopes) led the Division to sponsor a special round-table discussion of the subject in San Francisco in April, during the annual meetings of the Federation of American Societies for Experimental Biology and the American Association for Cancer Research. A subsequent conference, with emphasis on chemical, pharmacological, and biochemical problems of the lanthanons and yttrium, has been planned for the fall of 1955.

George T. Johnson, an Oak Ridge research participant from the University of Arkansas, has been using carbon-14 in a study of fatty-acid metabolism in the growth of molds. Another participant, M. K. Berkut, University of North Carolina, is engaged in making an evaluation of rubidium as a physiological substitute for potassium, which has no isotope of sufficiently long half-life for convenient long-distance shipping. Leon Singer, University of Minnesota, Mohammad Maqsood, Punjab College of Animal Husbandry, Lahore, Pakistan, and A. B. Medlin, A and M College of Texas, have been working on a study of calcium and strontium metabolism, chiefly in dogs.

Paper electrophoresis (the movement of suspended particles through a fluid through electromotive force) was applied to the study of body fluids of patients, to the study of uptake and transport of radioisotopes by body fluids, and to immunologic studies. A special investigation of the behavior of lutecium-177, using two methods of electrophoresis plus other analysis methods and animal experimentation, reveals that lutecium is electrophoretically transported in ascitic fluids of certain patients and not in others. Artificial mixtures of lutecium-177 with separated plasma fractions, amino acids, and other compounds have been examined for electrophoretic behavior; many definite data have been obtained and identification of complexing compounds is continuing. Principally responsible for the electrophoresis work has been Renaat Loos, an International Cooperation Administration participant from the University of Ghent, Belgium.

Dr. Loos, in collaboration with P. P. Levine, Oak Ridge research participant from New York State Veterinary College, has also been conducting research to determine a new rapid method for proving the immunity of chickens against infectious bronchitis, with a radioactive virus or radioactive serum. Interesting data were obtained on the influence of virus on the uptake and metabolism of phosphorus-32 and sulfur-35 in the embryo. It has been found, for instance, that the uptake of radioactive material in virus-infected eggs is seven to ten times greater in the embryos than in the egg fluids; conversely, in normal, noninfected eggs, most of the activity is concentrated in the fluids and comparatively little in the embryos.

Dr. Levine made an investigation to determine whether radioisotopes could be used in the problems of immunity to infection caused by coccidiae (intestinal parasitic protozoa) in birds. Birds that have been infected with coccidiosis and have recovered do show immunity to further infection, but the nature of the immunity is largely unknown. Although the project was hampered by the fact that the protozoa refused to accept the radioactive material, several facts were revealed: Large volumes of blood plasma from immune birds had no effect when administered to susceptible birds; intestinal tracts became immune only in areas that previously supported infection.

Attempts to grow the coccidia in tissue culture are still in progress, in collaboration with Major James Shively, US Army Veterinary Corps.

LOW-LEVEL COUNTING STUDIES

A survey to evaluate the levels of radioactive iodine in the human and livestock population in this country, as correlated with atomic-bomb fallout, has been undertaken by the Division, in an effort to anticipate potential hazards from atomic detonations and the effect, if any, on the diagnostic use of iodine. Two outside groups are collaborating in this study (see Appendix III), for which United States pathologists have been supplying human thyroids and the US Army Veterinary Corps has been sending cattle thyroids and other samples, as well as collaborating in some of the measurement. A study meeting with these groups was planned for July. Preliminary results indicate that radioiodine uptake in human beings is so low as to produce not the slightest physiological result or to in any way interfere with testing procedures; cattle values are somewhat higher, but still negligible. This survey will continue, to determine a base line between atomic tests.

The Division is taking advantage of certain new isotopes that are becoming available through bombardment with special instruments or from bombardments of separated stable isotopes. One of these new isotopes will be fluorine-18, a short-lived isotope which should be available in relatively large amounts from local calutron production. Another important new isotope will be calcium-47, which is also short-lived, and has the advantage of practical patient use, for which the long-lived calcium-45 is impossible.

CLINICAL STUDIES

The Division has conducted extensive investigations of intracavitary, intravenous, and interstitial administration of yttrium-90 and lutecium-177 – with and without added stable carrier – and with gold-198 (which is now considered practical rather than experimental). Tentative intracavitary results indicate that chloride of yttrium with added stable yttrium as a carrier remains satisfactorily localized. Intravenous administration of yttrium-90 also results in the predicted localization, chiefly in the reticuloendothelial organs; the carrier effect has not been striking in intravenous use as it has been in intracavitary and interstitial administration.

Gold-198 (which was used considerably) and intracavitary yttrium-90 with carrier appear to be favorable for controlling ascites and pleural effusions, although studies with the latter isotope are only preliminary and lack sufficient supporting data.

Radioactive-Iodine Studies

Continued study of selected cases of thyroid carcinoma has provided autoradiograms of functioning thyroid carcinoma after doses of radioiodine. Active interest has been expressed in thyroid and renal-clearance studies from both the theoretical and practical viewpoints, and some clarification and improvement of this method has been achieved. Concentrations of radioiodine in salivary glands has also been investigated to clarify the physiologic mechanisms involved, for which Zeth Gabrielsen, MD, Fulbright research scholar from the University of Bergen School of Medicine, has been chiefly responsible.

Because of the complexity of the situation, no conclusions have been drawn as to the effects of radioiodine and induced myxedema on patients with multiple myeloma; it appears that patients retain abnormal amounts of radioiodine, not correlated with either an increased thyroid concentration or significant localization in the myelomatous lesions.

Hematologic Disorders

A small group of patients with chronic granulocytic leukemia have been treated with intravenous colloidal gold-198, and a considerable number with polycythemia have received conservative therapy with radioactive phosphorus-32; plasma-volume and red-cell-mass studies

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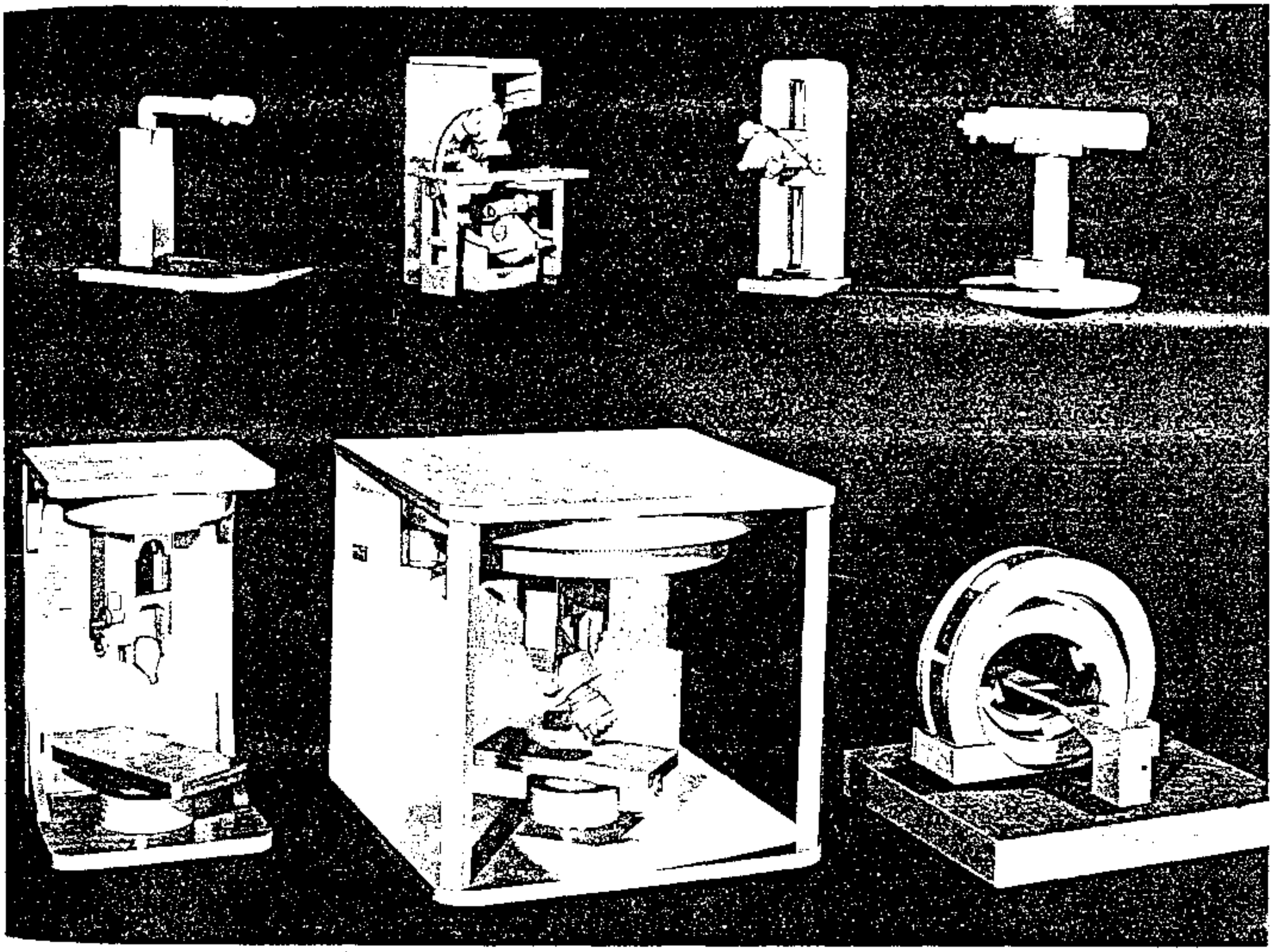
have been made of these patients. Red-cell-survival investigations, using iron-59, chromium-51, or both, have been conducted on a small group of patients with hematologic disorders.

Miscellaneous Studies

Two patients received multiple doses of strontium-85 for a special study of the metabolism of this isotope. Clinical investigations with labeled compounds of metabolic significance were made on a small number of patients; materials used included iodine-131-labeled thyroxin and rose bengal.

Instrumentation and Clinical Correlation

Improvements in equipment for external measurements of thyroid uptake and surgical probe counting were made during the year. Results from the scintiscanner (an electronic device for showing the location and concentration of radioactive material in tissue) were correlated with careful autoradiographic and assay studies, and attempts were made to define limits of usefulness of the machine. The chief impetus for these improved instruments was provided by an Oak Ridge National Laboratory group headed by P. R. Bell.



Models of teletherapy machines were prepared by the Medical Division for display at the United Nations Conference on the Peaceful Uses of Atomic Energy at Geneva. The models represent machines utilizing the following radiation sources (upper left to bottom right): europium-162 (curie); cobalt-60 (rotational); cobalt-60 (hectocurie); Jacobs-Li (hectocurie); cesium-137 (ceiling suspension); cesium-137 (moving field); and double cobalt-60 (moving field).

APPENDIX III

MEDICAL DIVISION

PUBLICATIONS FROM THE MEDICAL DIVISION (FISCAL YEAR 1955)

THE CLINICAL USE OF BONE-MARROW STUDY. G. A. Andrews. *Journal of the Tennessee State Medical Association*, Vol. 47, 1954, pages 361-366.

LOCALIZATION OF ANTIMONY IN BLOOD. C. T. Bahner. *Proceedings of the Society for Experimental Biology and Medicine*, Vol. 86, 1954, pages 371-373.

THE USE OF EXTERNAL RADIATION SOURCES, BETA AND GAMMA. M. Brucer. *Proceedings of the Second National Cancer Conference*, Vol. 2, 1952, pages 1647-1651.

STANDARDIZED COBALT-60 SOURCE CAPSULE FOR TELETHERAPY. M. Brucer, *Nucleonics*, Vol. 12, No. 6, 1954, pages 58-59.

A STANDARD COBALT-60 TELETHERAPY SOURCE CAPSULE. M. Brucer. *British Journal of Radiology*, Vol. 27, 1954, pages 410-412.

AN AVAILABLE COBALT-60 SOURCE FOR TELETHERAPY. M. Brucer. *Nucleonics*, Vol. 12, No. 8, 1954, pages 45-46.

MARBLE USED AS A RADIATION SHIELD. M. Brucer. *Marble Institute of America, Inc.*, 1954, pages 6-29.

MARBLE AS A RADIATION SHIELD. M. Brucer. *Nucleonics*, Vol. 13, No. 1, 1955, page 65.

THE DISTRIBUTION OF INTERSTITIAL AND INTRACAVITARY INJECTIONS OF CERTAIN RADIOCHEMICAL PREPARATIONS OF MEDICAL INTEREST. G. C. Kyker. *Bulletin of the Medical Association of Puerto Rico*, Vol. 46, 1954, pages 362-374.

LARGE DOSES OF IODINE-131 IN DOGS: RADIATION DOSAGE CORRELATED WITH HISTOLOGIC AND AUTORADIOGRAPHIC CHANGES. M. Levene, G. A. Andrews, and R. M. Kniseley. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine*, Vol. 73, 1955, pages 88-97.

INTEGRAL DOSE MEASUREMENTS; PRELIMINARY REPORT ON A COBALT-60 TELETHERAPY BEAM (abstract). L. D. MacDonald, R. L. Hayes, and M. Brucer. *Radiology*, Vol. 64, 1955, pages 115-116.

MODIFICATION OF ELECTRON FILTER TO IMPROVE LIGHT LOCALIZATION OF A COBALT-60 BEAM. J. E. Richardson and M. Brucer. *Radiology*, Vol. 64, 1955, pages 398-403.

SKIN DOSE FROM A COBALT-60 TELETHERAPY UNIT. J. E. Richardson, H. D. Kerman, and M. Brucer. *Radiology*, Vol. 63, 1954, pages 25-36.

THE DISTRIBUTION AND RADIATION EFFECTS OF INTRAVENOUSLY ADMINISTERED RADIOACTIVE COLLOIDAL GOLD-198 IN MAN. S. W. Root, G. A. Andrews, M. P. Tyor, and R. M. Kniseley. *Cancer*, Vol. 7, 1954, pages 856-866.

DISTRIBUTION OF COLLOIDAL RADIOACTIVE CHROMIC PHOSPHATE AFTER INTRACAVITARY ADMINISTRATION. S. W. Root, G. A. Andrews, M. P. Tyor, and R. M. Kniseley. *Radiology*, Vol. 63, 1954, pages 251-257.

HUMAN SERUM ALBUMIN TAGGED WITH IODINE-131 IN PATIENTS WITH ASCITES CAUSED BY ABDOMINAL CARCINOMATOSIS AND PORTAL CIRRHOSIS: THE RATES OF INTERCHANGE BETWEEN THE VASCULAR COMPARTMENT AND PERITONEAL CAVITY. M. P. Tyor. *Journal of Laboratory and Clinical Medicine*, Vol. 44, 1954, pages 110-117.

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Kenneth P. McConnell
Joe Bert Nash
Wiktor Waclaw Nowinski
Vernie Albert Stembridge
Howard G. Swann

M. D. Anderson Hospital

R. Lee Clark, Jr.
Gilbert H. Fletcher
Robert J. Shalek

Baylor University School of Medicine

Vincent Collins
Joseph Gast
Elliott B. Hay
John A. Isherwood
Harold Tivey

Jefferson Davis Hospital

R. Kenneth Loeffler

Virginia

Medical College of Virginia

Frederick B. Mandeville
George Zur Williams

University of Virginia

George Cooper
Kenneth R. Crispell
Chalmers L. Gemmill
George R. Minor

Wisconsin

University of Wisconsin

Edgar S. Gordon

Puerto Rico

University of Puerto Rico

Conrado Asenjo

RESEARCH PARTICIPANTS

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Aaron Ganz	University of Tennessee Memphis, Tennessee
Robert A. Woodbury	University of Tennessee Memphis, Tennessee
L. D. MacDonald	University of Mississippi University, Mississippi
Martin Levene	Lemuel Shattuck Hospital Jamaica Plain, Massachusetts

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D. A. Ross	University of Tennessee Memphis, Tennessee
Michael K. Berkut	University of North Carolina Chapel Hill, North Carolina
Leon Singer	University of Minnesota Minneapolis, Minnesota
George T. Johnson	University of Arkansas Fayetteville, Arkansas
Ammon B. Medlen	A and M College of Texas College Station, Texas
Marion T. Clark	Emory University Atlanta, Georgia

VISITING FOREIGN PERSONNEL

Kamal Mahmoud	University of Cairo Cairo, Egypt
Mamoon Magid	University of Cairo Cairo, Egypt
Renaat Loos	University of Ghent Ghent, Belgium

RESIDENT PHYSICIANS

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William C. Moloney	Duke University Durham, North Carolina
Dabney Ewin	Ochsner Clinic New Orleans, Louisiana
Ernest A. Daigneault	University of Tennessee Memphis, Tennessee
Frederick S. Tomchik	Massachusetts General Hospital Boston, Massachusetts

AIR FORCE RESIDENTS

John Schooly	United States Army Berkeley, California
Harry A. Weiss	United States Navy San Diego, California

SHORT-TERM MEDICAL STUDENTS

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Nelson Stephens	Meherry Medical School Nashville, Tennessee
S. Irwin Roth	Harvard Medical School Boston, Massachusetts
Herschel Estep	John Hopkins Medical School Baltimore, Maryland

FELLOWS

Fulbright Fellow

T. H. Oddie	University of Arkansas Little Rock, Arkansas

Damon Runyon Memorial Fund for Cancer Research Fellow

Chiyeko Okawa	St. Luke's International Hospital Tokyo, Japan

POST-RESIDENT STAFF MEMBERS

Paul M. St. Aubin	Department of Radiology Massachusetts General Hospital Boston, Massachusetts
James A. Petersen	Department of Radiology Massachusetts General Hospital Boston, Massachusetts
Walter P. Quigley	Department of Radiology Brooklyn Hospital Brooklyn, New York

ORINS HOSPITAL PATIENT-DAYS

July	413
August	555
September	387
October	184
November	308
December	284
January	390
February	354
March	437
April	320
May	235
June	450
Total patient-days	4317

PARTICIPANTS IN LOW-LEVEL COUNTING THYROID COLLECTION PROGRAM

E. A. Ballinger	Armed Forces Special Weapons Project Washington, D. C.
Walter Carll	US Army Veterinary Corps Oak Ridge, Tennessee
T. H. Cochran	University of Utah College of Medicine Salt Lake City, Utah
James R. Dawson, Jr.	University of Minnesota Medical School Minneapolis, Minnesota
Nathan B. Friedman	Cedars of Lebanon Hospital Los Angeles, California
U. S. Grant Kuhn, III	US Air Force Veterinary Corps Oak Ridge, Tennessee
Marvin Kuschner	Bellevue Hospital Center New York City
Roy D. Maxwell	Armed Forces Special Weapons Project Washington, D. C.
Kenneth P. McConnell	Veterans Administration Hospital Louisville, Kentucky
Max Nold	US Air Force Veterinary Corps Oak Ridge, Tennessee
Leopold Reiner	Beth Israel Hospital Boston, Massachusetts
James Shively	US Army Veterinary Corps Oak Ridge, Tennessee

Vinton D. Sneeden	Emanuel Hospital Portland, Oregon
Walker B. Sorrell	Tulane University School of Medicine New Orleans, Louisiana
Vernie Stembridge	University of Texas Medical Branch Galveston, Texas
Bernard F. Trum	US Army Veterinary Corps Oak Ridge, Tennessee

TELETHERAPY EVALUATION PROGRAM

Institution	Representative on TEP
Baylor University	Vincent Collins
Creighton University	James F. Kelly, Jr.
Duke University	Robert J. Reeves
Emory University	H. Stephen Weens
Louisiana State University	Walter J. Burdette
Medical College of Virginia	Frederick B. Mandeville
New York University (Bellevue Medical Center)	Sidney Rubenfeld
State University of New York (Syracuse)	Alfred S. Berne
University of Alabama	William H. Riser, Jr.
University of Arkansas	I. Meschan
University of Kansas	Galen M. Tice
University of Louisville	Herbert D. Kerman
University of Mississippi	A. C. Guyton
University of Nebraska	Howard B. Hunt
University of Southern California	Henry L. Jaffe
University of Tennessee	David S. Carroll
University of Texas (Medical Branch, Galveston)	Robert N. Cooley
University of Texas (M.D. Anderson Hospital)	Gilbert H. Fletcher
University of Virginia	George Cooper
Vanderbilt University	C. C. McClure
Wake Forest College	
Wayne University	James E. Lofstrom

COMMITTEES OF THE TELETHERAPY EVALUATION PROGRAM

Executive Committee (elected by the TEP)

Serving second year of two-year term:

Vincent Collins	Baylor University
Henry L. Jaffe	University of Southern California
James E. Lofstrom	Wayne University
Carl E. Nurnberger	University of Tennessee

Elected to serve two years:

I. Meschan	Wake Forest College
David S. Carroll	University of Tennessee

Elected to serve one year:

Marshall Brucer	OR Institute of Nuclear Studies

Subcommittees (appointed by the executive committee)

No. 1. Source Evaluation and Shield Design

Herbert D. Kerman	University of Louisville
David S. Carroll	University of Tennessee
Carl E. Nurnberger	University of Tennessee
John Tolan	Emory University

No 2. Small Source Design

Henry L. Jaffe	University of Southern California
John Isherwood	Brooke Army Medical Center, Fort Sam Houston
James F. Kelly, Jr.	Creighton University
H. Stephen Weens	Emory University
Harold W. Lewis	Duke University

No. 3. Rotational Methods

Kenneth Loeffler	Jefferson Davis Hospital, Houston
J. Robert Andrews	Bowman Gray School of Medicine
Frederick B. Mandeville	Medical College of Virginia
C. C. McClure	Vanderbilt University

No. 4. Housing Design

James E. Lofstrom	Wayne University
Paul A. Riemenschneider	State University of New York (Syracuse)
Robert J. Reeves	Duke University
Sidney Rubenfeld	New York University (Bellevue Medical Center)

No. 5. Clinical Program

Vincent Collins	Baylor University
Isadore Meschan	University of Arkansas
George Cooper	University of Virginia
Galen M. Tice	University of Kansas
Herbert D. Kerman	University of Louisville

No. 6. Clinical Physicist Training Program

Frank Hoecker	University of Kansas
Walter J. Burdette	Louisiana State University
William H. Riser	University of Alabama
Howard B. Hunt	University of Nebraska
Arthur C. Guyton	University of Mississippi

Marshall Brucer, ORINS Medical Division, Chairman of the TEP, is a member *ex officio* of all subcommittees.

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TOPES USED BY THE MEDICAL DIVISION

Isotope	*mc*
Barium-132	13.85
Calcium-45	25
Cesium-137	50.1
(+ 1540-curie source for teletherapy unit)	
Chromium-51	13
Cobalt-60	5
Cobalt-60 (for brachytherapy)	3978
Europium-152, 154 (Cobalt-60 equivalent)	approximately 350
Gallium-67	382
Gold-198	7875
Holmium-166	260
Iodine-130	approximately 100
Iodine-131	3495
Iodine-131-labeled thyroxine	1
Iron-55	460
Iron-59	1
Lutecium-177	1746
Neodynium-147	0.2
Palladium-109	*
Phosphorus-32	283
Potassium-42	137
Praseodymium-142	3
Rubidium-86	242
Selenium-75	10
Strontium-89	150
Sulfur-35	65
Tellurium-130	*
Tellurium I-132	440
Yttrium-90	490
Yttrium-91	*

*Amount undetermined

6/30/56

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Tenth Annual Report

of the

Oak Ridge Institute of Nuclear Studies

OPERATING UNDER CONTRACT

with the

United States Atomic Energy Commission

and the

National Science Foundation

JUNE 30, 1956

Medical Division

THE Medical Division's year was characterized by the continuation of its regular programs as well as the development of several new programs from the drawing-board to the practical stages.

One of the largest physical manifestations of the division's activity was the addition of a

take-calibration methods employed by the various institutions.

The division held a conference on "Rare Earths in Biochemical and Medical Research" October 27-29, with Granvil C. Kyker, chief of laboratory research, acting as program chairman. Attendance totaled approximately

Division staff members also spoke on the program presented for the meeting of the AEC Biomedical Program Directors, held in Oak Ridge May 31–June 2. The division's regular clinical conference on May 31 was slightly modified to accommodate the physician members at the meeting, and a special conference was held at the division on June 1 for an informal discussion of equations for the life-shortening effects of irradiation on large mammals.

In June, the Atomic Energy Commission issued an 817-page book, "Radioisotopes in Medicine," which is the complete proceedings of a course on the subject, which was conducted by the Medical Division in the fall of 1953. The book contains 48 chapters, divided into nine main sections, complete with bibliography, index, charts, and illustrations. Editors are Gould A. Andrews, Marshall Brucer, and Elizabeth B. Anderson of the Medical Division.

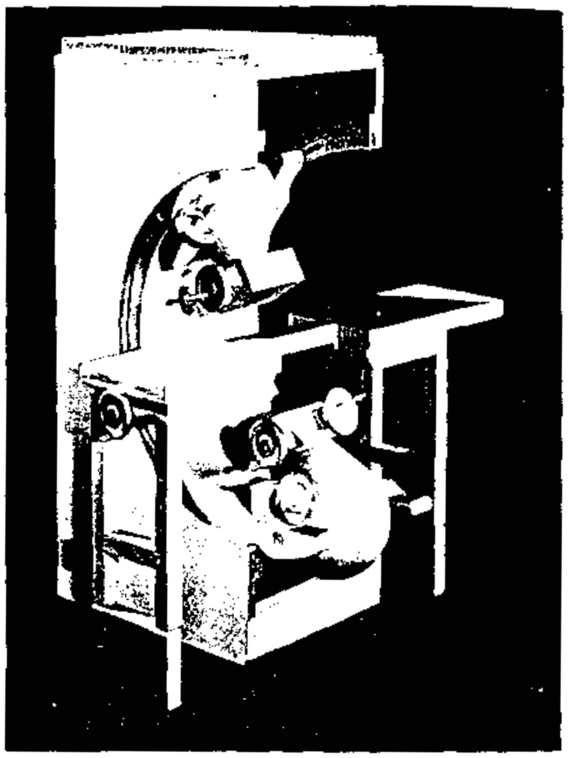
The work of the Medical Division for the past year was presented June 7 in Washington, D. C., before the Joint Committee on Atomic Energy, whose hearings will be published in the near future.

TELETHERAPY PROGRAM

Installation and preliminary testing of the division's cesium-137 teletherapy machine was conducted during the 1954–55 fiscal year. This year a continuous series of isodose-plotting tests were carried out with the machine to determine dose rates to diseased tissue during various rotational patterns; the results of these tests will be evaluated upon completion of the series, to ascertain optimum patterns and dosage times for varying conditions.

Late this year, a program was initiated, under the direction of assistant scientist Francisco Comas, to use the cesium-137 and cobalt-60 machines in the experimental treatment of a small number of selected patients with neoplasma.

Throughout the year, a number of discussions were held with representatives of the Westinghouse Electric Company concerning a new, rotational, cobalt-60 teletherapy machine that Westinghouse is building for ORINS. Because the major portion of the problems attendant upon the design and construction of cobalt-source machines, as well as the problems con-



Model of a teletherapy machine for use with cobalt-60 or cesium-137. This machine was designed under contract by the Westinghouse Electric Company and ORINS as a low-cost unit with a simplified control system.

nected with the characteristics of cobalt-60 itself, have been solved, the new machine will be relatively economical. By the end of the year, the unit had been completely designed, and construction of experimental models was in progress.

Two contracts have been negotiated with the W. F. and John Barnes Company for the design and construction of teletherapy units of extremely small size, as opposed to the general trend toward larger and larger machines. This program is still largely in the discussion stage.

The division has made extensive calculations of integral dose in rotational teletherapy; it has been established that integral dose with a beam of constant solid angle is largely independent of body shape, and is principally determined by irradiation time. A study was made of the variation of integral dose with ra-

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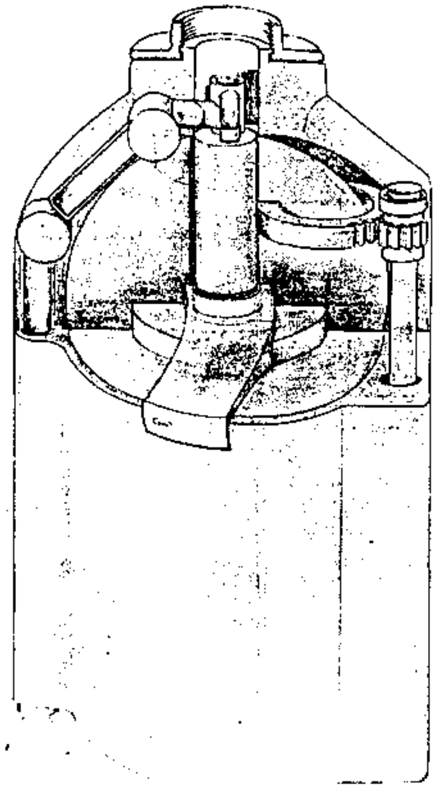
diation energy, and has resulted in the simplification of calculation of integral dose in complex rotational treatments.



Sketch of a contemplated special-purpose teletherapy machine for low-energy radiation.

BRACHYTHERAPY PROGRAM

A conference on brachytherapy (close source-to-tissue distance) was held at the Medical Division on July 8, 1955, attended by 14 physicians from institutions throughout the country. One of the major items on the agenda was a recommendation to the ORINS Board of Directors that a brachytherapy program be initiated by the Medical Division.

The principal subject of discussion was the use of the International Nickel Company's "Incoray" alloy (a mixture of nickel, chromium, molybdenum, aluminum, and cobalt) in brachytherapy devices. Incoray appears to produce extremely low contamination when embedded in subcutaneous tissue, or placed in feces, urine, and blood; this property seems to make it far superior to other forms of irradiated cobalt used in brachytherapy, which must be encapsulated to reduce tissue contamination. Much of the expense incurred in using radiocobalt in brachytherapy devices arises from this encapsulation provess; hence, Incoray could be much more economical and versatile than other cobalt-therapy devices.

The Brachytherapy Committee recommended testing various types of Incoray brachytherapy devices to establish a uniform clinical program of evaluation and continuation by the division of a limited program of manufacture and clinical testing of various brachytherapy devices. (The clinical testing would be carried out in a selected group of universities and teaching hospitals.)

At several other meetings of the Brachytherapy Committee during the year, a large number of other brachytherapy devices were discussed; some of these are being manufactured with the cooperation of the Bowman Gray School of Medicine, Massachusetts General Hospital, and other institutions.

THYROID UPTAKE CALIBRATION

At the end of the year, the division has almost completed Phase One of the thyroid-uptake-calibration program—the circulation to research institutions about the country of half-body mannequins with simulated thyroid glands containing mock-iodine, for calibration by local scientists and physicians, with the eventual objective of standardizing measurement techniques for more accurate results. (Mock-iodine is a mixture of radioactive barium and cesium having radiation characteristics similar to those of iodine-131, with the further advantage of a useful life of more than ten years.)

Work is now in progress to prepare for Phase Two of the program—a comparison of the hundreds of readings and techniques reported by the assisting scientists. Phase Two will be initiated in September of 1956, utilizing the facilities of a new clinical-training wing which was completed this year.

A considerable portion of the preliminary work to Phase Two has been conducted by Hirotake Kakehi, nonemployee visitor from Tokyo University. Other important contributions have been made by Fearghus O'Foghludha, nonemployee visitor from Dublin, Ireland; Kuang-Chu Wang, nonemployee visitor from Formosa; and Douglas A. Ross, staff research scientist.

The Thyroid Uptake Calibration Committee met in Oak Ridge October 14, 1955, to discuss the results received to date in Phase One of the survey and to suggest improvements in instrumentation and techniques for the survey.

A 20-channel pulse-height analyzer and scintillation probe were used to study degradation and absorption of iodine-131 radiation emerging from the human thyroid. The measurements were used to design a phantom which degrades and absorbs iodine-131 radiation in a manner similar to that of the human neck; the use of this phantom is expected to produce a great improvement in the accuracy and consistency of thyroid-uptake measurements.

Marshall Brucer, chairman of the division, confers with Hirotake Kakehi, a Fulbright Fellow from Japan who is spending a year at the ORINS Medical Division to investigate methods of measuring radioisotopes used in medical practice. A point source of mock-iodine (a mixture of barium-133 and cesium-137) is used to map out the "visual field" of a counting system before it is used on a patient.

In connection with the thyroid-uptake survey, a density-measurement calibration survey has been carried out by the Medical Division, working through a subcommittee of the American Society for Testing Materials. A large number of institutions where density measurements are carried out have been surveyed, and it is expected that the program will be completed in the near future.

THYROID-COLLECTION PROGRAM

The program of collecting human and livestock thyroids has been continued throughout the year. These glands have been analyzed for radioactivity to determine the contamination of the biological cycle caused by nuclear weapons tests carried out by various countries. Detectable amounts of activity have been found and correlated with the various test series. The amounts of radiation detected have proved to be so small as to constitute no hazard. In general, the values for humans are many times lower than those for grazing animals. The study is to be continued in order to provide a background of information on the radioactivity level as time goes on.

BIOMEDICAL RESEARCH

The metabolism of strontium-85 has been studied in several patients, and has provided interesting information in regard to the metabolism of calcium and strontium under conditions of bone disorders. The information is also of interest in connection with the possible hazards of other isotopes of strontium from fallout. Corollary information has been obtained on the effect of the particular disease condition and the nutrition of the patients.

Preliminary studies have demonstrated the feasibility of using silver phosphate-glass dosimeters for the measurement of doses delivered to the lining of the digestive tract from insoluble radioactive material that has been ingested.

A program of study on radiation-protection measures has been conducted for the past year by a group headed by Jean D. Mewissen, nonemployee visitor from the University of Liege,

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Belgium. One portion of the program, conducted at the Medical Division, is concerned with the protective action of betamercaptoethylamine on gamma-irradiated mice, and the fate of these mice after they have passed the early-death period experienced by unprotected, irradiated mice. The study is largely concerned with the incidence of leukemia in the surviving mice, as a result of observations made on survivors of the Hiroshima and Nagasaki nuclear explosions. Results to date indicate that mice that survive irradiation because of treatment with protective agents have a greater tendency to develop lymphoma in the postirradiation period.

One theory for the increase in lymphoma incidence is the possibility that the protective substance might itself be a cocarcinogenic agent; study has shown that this is not the case. Further studies showed that the increased incidence of tumor cannot be accounted for by the increased survival in the protected group.

In another experiment, an investigation was made on the protective action of certain substances with internally administered radioisotopes. A moderate degree of protection was afforded by cystamine (disulfide of betamercaptoethylamine) in some experiments with phosphorus-32.

Part of Dr. Mewissen's work for the Medical Division was carried out in cooperation with the University of Tennessee-Atomic Energy Commission Agricultural Research Program, where the effect of large amounts of external radiation on large animals and the extrapolation of these effects on man was studies. As a result, a new mathematical formula has been developed to relate mortality to the dosages of chronic gamma irradiation applicable to large mammals.

LABORATORY RESEARCH

Activities of Visiting Personnel

Renaat Loos, nonemployee visitor from the University of Ghent, Belgium, has been conducting electrophoretic tracer studies of rare earths with components of serum and plasma in laboratory animals. The program is a survey involving the use of four rare earths in different preparations and increasing dose levels, to study the components with which the rare earths react in the animal. Results indicate prominent complexing by plasma constituents; the patterns for the different rare earths have several similar characteristics. The biological half-times of the different complexes have been studied. A detailed final report on this experimental work is nearing completion.

George T. Johnson, research participant from the University of Arkansas, has been spending the summer continuing a study begun in the summer of 1955 on a growth problem with Spicaria Violacea, an organism which can obtain its organic nutritional needs from a pure fat. Dr. Johnson has been using carbon-14-labeled fatty acids to study the fat metabolism of this organism; results have shown that all the fatty-chained acids with up to seven carbon atoms support growth, as do the higher fatty acids with 14 to 18 carbon atoms. This study represents both a basic study of growth and a fundamental study of Spicaria Violacea.

Michael K. Berkut, research participant from the University of North Carolina, is engaged in a study of the role of potassium in the process of mineralization. He has used radioisotopes of potassium and of rubidium in both single and in double isotope experiments. The localization of potassium in cartilage and hard bone as a function of time and age of the animal was compared with that of rubidium. Also, he has compared the renal-excretory rates of rubidium-86 and potassium-42 to evaluate similarity in behavior, as a possible development of clinical diagnostic tests for potassium, using the rubidium isotope.

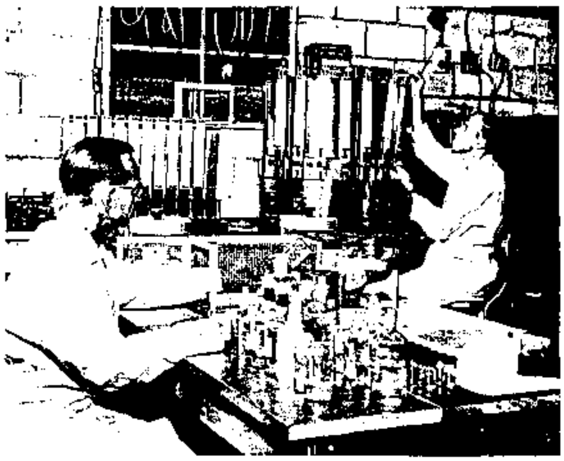
Activities of Technical Staff

The regular staff has continued basic studies of rare earths in laboratory animals. These studies include effects on the liver tissue as reflected by oxygen consumption. Prominent injury has been observed metabolically and histologically, following intravenous administration of mixed rare earths to rats.

The role of mixed heterogeneous carriers has been studied in mice and found to have a similar effect on distribution of that of various individual carriers described in previous reports.

In larger animals, the disappearance of different rare earths from circulating blood has been studied by tracer techniques. In general, an increase in the dose tends to increase the biological half-time of the circulating fraction of the dose.

In collaboration with the Departments of Pathology and Surgery, University of Louisville, three preparations of lutecium have been



Several Medical Division programs are carried out in laboratories located at the University of Tennessee-Atomic Energy Commission Agricultural Research Program in Oak Ridge. Above, Granvil C. Kyker, chief of laboratory research (left), removes an experimental rat from its cage while research associate Ed Cress operates a Warburg respirometer. The rat is one of many undergoing metabism studies of liver slices following experimentation with rare-earth elements.

compared by the intramammary route in dogs. Favorable localization of radiolutecium in the lymph nodes of the area is observed. Less damage to the primary site is noticed than with radiogold.

CLINICAL STUDIES

Continued studies with yttrium-90 and lutecium-177, particularly for intracavitary administration, indicate that these isotopes remain very well localized in the region of body cavities when given with added stable yttrium as carrier. Evaluation of therapeutic results has been difficult, and it is felt that, as yet, no adequate comparison can be made between the newer isotopes and gold-198. In a very few patients, interstitial injections of yttrium-90 and lutecium-177 have been given; there is some indication that they may show a greater tendency to travel in lymphatics than do radioactive chromic phosphate (phosphorus-32) and colloidal radiogold, but this has not been clearly established in the human studies. Intravenous injection of yttrium-90 and lutecium-177 has indicated that they do not have as rapid clearance from the blood as colloidal gold-198.

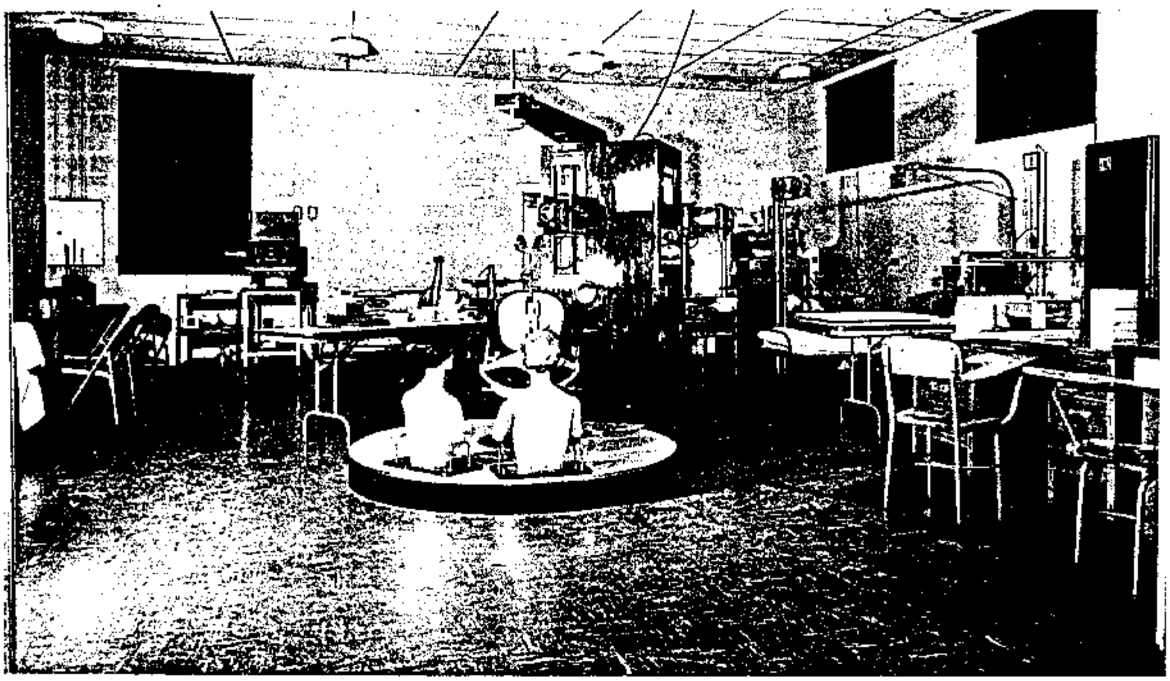
Studies have been discontinued with radioactive iodine-131 in multiple myeloma and a final evaluation of the results is in progress; there appears to be no evidence that iodine-131 localizes significantly in myeloma lesions, nor that it offers a desirable form of therapy. Other radioactive-iodine studies have continued: Two unusual patients showing a clear cell transformation of well-differentiated thyroid carcinoma following removal of normal thyroid tissue have been studied in detail, and a report has been submitted to American Journal of Clinical Pathology.

The division has continued to study and evaluate a considerable number of patients with carcinoma of the thyroid. The scintiscanner with recent improvements of pulse-height selection and focusing collimators has been used extensively in studying such problems. Even with the distinct improvements of these recent innovations, the scintiscanner seems to give less detailed information than has often been reported; nevertheless, the instrument is of great practical value in certain cases, such as evaluating the success of surgery in removing total thyroid gland.

Studies on the thyroid clearance of iodine-131 have been continued and a special method has been worked out for making allowance for the radioiodine in the nonthyroid structures of the neck.

Studies on radioactive phosphorus, in progress since the beginning of the Medical Division's clinical program, have produced an extensive amount of data on the distribution of radiophosphorus in various types of neoplasms. Evaluation of these data emphasizes the very general distribution of phosphorus-32. The high concentration in epiphysis of growing children was not fully appreciated in earlier studies. Phosphorus tends to concentrate in growing-bone areas, and radioassays of large bone areas, containing both growing and non-growing bone, give average figures considerably lower than those obtained by localized radioassays of growing-bone areas. Except for these growing-bone areas, the liver is consistently the organ having the highest concentration of radioactive phosphorus. In general, these studies with radioactive phosphorus do not offer encouragement for the use of this isotope, except in those diseases that respond to total-body irradiation; however, there is some current interest in the use of radioactive phosphorus in certain types of bone metastases, and the data available here should be of value in interpreting this type of therapeutic use.

The clinical staff of the Medical Division has continued to be interested in a wide variety of hematologic disorders, and an increasing number of patients have been seen on referral from other physicians in this area. In addition to the use of radioactive phosphorus and intravenous colloidal gold-198, the division has utilized various chemotherapeutic agents. There has been a continued interest in the use of hematologic changes and bone-marrow changes in the evaluation of radiation.



The instrument room in the new training wing of the Medical Division.

APPENDIX III
Medical Division

TELETHERAPY EVALUATION PROGRAM

Institution	Representative on TEP
Baylor University	Vincent Collins
Creighton University	James F. Kelly, Jr.
Duke University	Robert J. Reeves
Emory University	H. Stephen Weens
Louisiana State University	Walter J. Burdette
Medical College of Virginia	Frederick B. Mandeville
New York University (Bellevue Medical Center)	Sidney Rubenfeld
State University of New York (Syracuse)	Paul Riemenschneider
University of Alabama	William H. Riser, Jr.
University of Arkansas	Howard J. Barnhard
University of Kansas	Galen M. Tice
University of Louisville	Ji-toong Ling
University of Mississippi	Robert D. Sloan
University of Nebraska	Howard B. Hunt
University of Southern California	Henry L. Jaffe
University of Tennessee	David S. Carroll
University of Texas (Medical Branch, Galveston)	Robert N. Cooley
University of Texas (M.D. Anderson Hospital)	Gilbert H. Fletcher
University of Virginia	George Cooper
Vanderbilt University	
Wake Forest College	I. Meschan
Wayne University	James E. Lofstrom

PARTICIPANTS IN LOW-LEVEL COUNTING THYROID COLLECTION PROGRAM

E. A. Ballinger	Armed Forces Special Weapons Project, Washington, D. C.
Walter Carli	US Army Veterinary Corps, Oak Ridge, Tennessee
T. H. Cochran	University of Utah College of Medicine, Salt Lake City, Utah
James R. Dawson, Jr.	University of Minnesota Medical School, Minneapolis, Minnesota
Nathan B. Friedman	Cedars of Lebanon Hospital, Los Angeles, California
U. S. Grant Kuhn, III	US Air Force Veterinary Corps, Oak Ridge, Tennessee
Marvin Kuschner	Bellevue Hospital Center, New York, New York
Roy D. Maxwell	Armed Forces Special Weapons Project, Washington, D. C.
Kenneth P. McConnell	Veterans Administration Hospital, Louisville, Kentucky
Max Nold	US Air Force Veterinary Corps, Oak Ridge, Tennessee
D. G. Freiman	Beth Israel Hospital, Boston, Massachusetts
Vinton D. Sneeden	Emanuel Hospital, Portland, Oregon
N. J. Chetta	New Orleans, Louisiana
J. H. Childers	University of Texas Medical Branch, Galveston, Texas
Bernard F. Trum	US Army Veterinary Corps, Oak Ridge, Tennessee

CONSULTANTS TO THE MEDICAL DIVISION

ALABAMA

Medical College of Alabama
Champ Lyons
William H. Riser

ARKANSAS

University of Arkansas Medical Center
Howard J. Barnhard

CALIFORNIA

Cedars of Lebanon Hospital
Stanley H. Clark
City of Hope Medical Center
Melville L. Jacobs
Eden Hospital
Ralph M. Kniseley
Los Angeles Veterans Administration Center
Franz K. Bauer
Raymond L. Libby
University of California at Los Angeles
Benedict Cassen
University of Southern California School of Medicine
Henry L. Jaffe

COLORADO

University of Colorado
Jerry K. Aikawa

FLORIDA

Florida State Board of Health
Lorenzo L. Parks
Halifax District Hospital
Herbert D. Kerman
Private Physicians
Louis M. Orr
Samuel W. Root
University of Florida
George T. Harrell
Francis C. Ray

GEORGIA

Emory University School of Medicine
Harry D. Bruner
Frank E. Morgan, Jr.
Bryan Redd
John H. Tolan
H. Stephen Weens
University of Georgia School of Medicine
Stephen W. Brown
Hoke Wammock
Medical College of Georgia
Claude-Starr Wright

ILLINOIS

Cook County Hospital
Irvin F. Hummon

KANSAS

University of Kansas
Frank E. Hoecker
University of Kansas School of Medicine
Galen M. Tice

KENTUCKY

University of Louisville School of Medicine
Harold F. Berg
J. Ray Bryant
William M. Christopherson
Hampden C. Lawson
Ji-toong Ling
Kenneth P. McConnell
Veterans Administration Hospital
David Shapiro

LOUISIANA

Ochsner Clinic
William R. Arrowsmith
Paul J. Murison
Tulane University
John U. Hidalgo
Robert T. Nieset

MARYLAND

National Institutes of Health
George Z. Williams

MASSACHUSETTS

Harvard University Medical School
A. Stone Freedberg
Massachusetts General Hospital
Paul M. St. Aubin

MICHIGAN

University of Michigan School of Medicine
Jere Bauer
Wayne County General Hospital
W. W. Glas
Lyndon E. Lee
Wayne University College of Medicine
S. L. Balofsky
James E. Lofstrom

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Arthur C. Guyton
Robert D. Sloan

MISSOURI

Private Physician
Wendell G. Scott
University of Missouri School of Medicine
Walter J. Burdette

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Creighton University School of Medicine
James F. Kelly, Jr.
University of Nebraska
Howard B. Hunt
Arthur Tuma

NEW YORK

Francis Delafield Hospital
Carl B. Braestrup
S. Allan Lough
Hospital for Joint Diseases
Milton Friedman
Naval Medical Research Institute
H. C. Dudley
New York University -- Bellevue Center
Sidney Rubenfeld
Private Physician
Norman Simon
State University of New York
G. Ferlazzo
Syracuse Memorial Hospital
Alfred S. Berne
Paul A. Riemenschneider

NORTH CAROLINA

Bowman Gray School of Medicine
Camillo Artom
Isadore Meschan
Thomas H. Oddie
Ernest H. Yount
Duke University School of Medicine
William G. Anlyan
Wilburt C. Davison
Philip Handler

Jerome S. Harris
Harold W. Lewis
Robert J. Reeves
C. R. Stephens
Malcolm P. Tyor

University of North Carolina
M. K. Berkut
John H. Ferguson
Cornelius T. Kaylor
Charles D. Van Cleave

NORTH DAKOTA

University of North Dakota School of Medicine
William E. Cornatzer

OREGON

University of Oregon Medical School
Carl Hopkins

PENNSYLVANIA

Temple University School of Medicine
R. C. Baldridge

SOUTH CAROLINA

Medical College of the State of South Carolina
John C. Hawk
William M. McCord

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Carson Newman College
Carl T. Bahner

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Paul C. Aebersold

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Robert R. Bigelow
Dana W. Nance
W. W. Pugh, Jr.
C. J. Speas
Paul E. Spray

University of Tennessee College of Medicine
David S. Carroll
Alfred P. Kraus
Carl E. Nurnberger
Jesse D. Perkinson, Jr.
John L. Wood
Robert A. Woodbury

Vanderbilt University
Herbert Francis
Granville Hudson
C. C. McClure

Veterans Administration Hospital
George R. Meneely

TEXAS

M. D. Anderson Hospital
R. Lee Clark, Jr.
Gilbert H. Fletcher
Robert J. Shalek

Baylor University
Vincent Collins
Elliott B. Hay
Harold Tivey

Brooke Army Medical Center
J. A. Isherwood

Jefferson Davis Hospital
R. Kenneth Loeffler

University of Texas Medical Branch
Ludwik Anigstein
Robert N. Cooley
Wendell D. Gingrich
William C. Levin
Wiktor W. Nowinski
Martin Schneider
Vernie A. Stembridge
Howard G. Swann

VIRGINIA

Medical College of Virginia
Frederick B. Mandeville

University of Virginia
George Cooper
Kenneth R. Crispell
George R. Minor

WISCONSIN

University of Wisconsin
Edgar S. Gordon

PUERTO RICO

University of Puerto Rico
Conrado Asenjo

ISOTOPES USED BY THE MEDICAL DIVISION

Isotope	mc
Cadmium-109	80
Calcium-45	135
Cesium-132 - Barium-137	400
Cerium-144	106
Cobalt-60	*
Europium-152,154	*
Gold-198	2,039.25
Holmium-166	489.42
Iodine-131-P	2,420
Iron-59	0.25
L-Thyroxine (I-131)	6.58
Lutecium-177	approximately 2,925
Mercury-203	2
Neodymium-147	5.295
Potassium-42	58.5
Rachromate (Cr-51)	10
RISA (I-131)	17
Rose Bengal (I-131)	46
Rubidium-86	135
Silver-110	1
Sodium-24	5
Sodium Iodide (I-131)	45
Sodium Phosphate (P-32)	240
Strontium-85	2.5
Strontium-89	15

*Amount undetermined

Tracervial (I-131)	2
Yttrium-90	855.93
Yttrium-91	50

PUBLICATIONS FROM THE MEDICAL DIVISION (FISCAL YEAR 1956)

Andrews, Gould A.

THE INTRAPLEURAL USE OF RADIOACTIVE COLLOIDAL MATERIALS. In: Therapeutic Use of Artificial Radioisotopes. Edited by Paul F. Hahn. John Wiley & Sons, Inc. 1956. Chapter 14, pp. 295-315.

Andrews, Gould A., Kniseley, Ralph M.,* Palmer, Etna L., and Kretchmar, Arthur L.

THERAPEUTIC USEFULNESS OF RADIOACTIVE COLLOIDS: COMPARATIVE VALUE OF GOLD-198, CHROMIC PHOSPHATE (P-32), YTTRIUM-90, AND LUTECIUM-177. International Conference on the Peaceful Uses of Atomic Energy. A/CONF. 8/P/184, USA, June 23, 1955.

Andrews, Gould A., Kniseley, Ralph M.,* Palmer, Etna L., and Kretchmar, Arthur L.

THERAPEUTIC USEFULNESS OF RADIOACTIVE COLLOIDS: COMPARATIVE VALUE OF GOLD-198, CHROMIC PHOSPHATE (P-32), YTTRIUM-90, AND LUTECIUM-177. In: Peaceful Uses of Atomic Energy: Proceedings of the International Conference in Geneva, August, 1955. Volume 10. Radioactive Isotopes and Nuclear Radiations in Medicine. United Nations. New York, 1956. pp. 122-137.

Bahner, Carl Tabb

EFFECT OF COMPOUNDS RELATED TO 4-(p-DIMETHYLAMINOSTYRYL) QUINOLINE METHIODIDE ON LYMPHOMA 8. Cancer Research 15, 588-592, October 1955.

Bahner, Carl Tabb

COLORIMETRIC STUDY OF ABSORPTION AND EXCRETION OF 4-(p-DIMETHYLAMINOSTYRYL) QUINOLINE METHIODIDE AND RELATED COMPOUNDS. Proc. Soc. Exper. Biol. & Med. 90, 133-135, 1955.

Brucer, Marshall

SPECIAL REPORT OF THE MEDICAL DIVISION ON TELETHERAPY DESIGN PROBLEMS I. Cs-137. TIS-5086 (2nd Rev.) May 15, 1955. Available from the Office of Technical Services, Department of Commerce, Washington 25, D. C. Price: 40 cents.

Brucer, Marshall

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Brucer, Marshall

AN AUTOMATIC CONTROLLED PATTERN CESIUM TELETHERAPY MACHINE. Am. J. Roentgenol. 75, 49-55, 1956.

Brucer, Marshall

TELETHERAPY DEVICES WITH RADIOACTIVE ISOTOPES. In: Peaceful Uses of Atomic Energy: Proceedings of the International Conference in Geneva, August, 1955. Volume 10. Radioactive Isotopes and Nuclear Radiations in Medicine. United Nations. New York, 1956. pp. 68-74.

Brucer, Marshall

TELETHERAPY DEVICES WITH RADIOACTIVE ISOTOPES. International Conference on the Peaceful Uses of Atomic Energy. A/CONF. 8/P/179, USA, June 23, 1955.

Brucer, Marshall

TELETHERAPY DEVICES WITH RADIOACTIVE ISOTOPES. TIS-8007. Technical Information Service, Washington, D. C. March, 1956. 10 pp.

Brucer, Marshall, et. al.

TELETHERAPY DESIGN PROBLEMS III, with supplement: PROCEEDINGS OF THE THIRD INDUSTRIAL CONFERENCE ON TELETHERAPY. ORO-127 and ORO-127 (Suppl.) 1954. For sale by the Superintendent of Documents, United States Government Printing Office, Washington 25, D. C. Price: 50 cents and 35 cents. Second printing.

Brucer, Marshall, Eldridge, James S., and Trombka, Jack

THYROID RADIOIODINE UPTAKE CALIBRATION. International Conference on the Peaceful Uses of Atomic Energy. A/CONF. 8/P/196, USA, June 23, 1955.

*Present address:
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Brucer, Marshall, Eldridge, James S., and Trombka, Jack

THYROID RADIOIODINE UPTAKE CALIBRATION. In: Peaceful Uses of Atomic Energy: Proceedings of the International Conference in Geneva, August, 1955. Volume 10. Radioactive Isotopes and Nuclear Radiations in Medicine. United Nations. New York, 1956. pp. 359-364.

Brucer, Marshall, Kerman, Herbert D.,* and Richardson, Jasper E.

TELETHERAPY DESIGN PROBLEMS II. COBALT-60 TELETHERAPY UNIT. ORO-109. For sale by the Superintendent of Documents, United States Government Printing Office, Washington 25, D. C. Price: 35 cents. Second printing.

Comar, C. L.

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Comar, C. L.

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Harris, Norman O., and Hayes, R. L.

A TRACER STUDY OF THE EFFECT OF ACUTE AND CHRONIC EXPOSURE TO SODIUM FLUORIDE ON THE THYROID IODINE METABOLISM OF RATS. J. Dent. Research 34, 470-477, August 1955.

Hayes, R. L., Brucer, Marshall, and Arakawa, Edward

SOME INTEGRAL DOSE RELATIONSHIPS IN CO-60 TELETHERAPY. Abstract 64. Radiation Research 3, October 1955.

Kyker, G. C., Rafter, J., Cress, E. A., and Stevens, N.

RADIOYTTRIUM WITH COMPLEX HETEROGENEOUS CARRIER. Abstr. 961. Federation Proc. 15, 1956.

*Present address:
Herbert D. Kerman
Halifax District Hospital
Daytona Beach, Florida

Totter, J. R. and Comar, C. L.

FUNCTION OF MOLYBDENUM IN XANTHINE OXIDASE. In: A Symposium on Inorganic Nitrogen Metabolism. Edited by William D. McElroy and Bentley Gloss. The Johns Hopkins Press, Baltimore, 1956.

RADIOISOTOPES IN MEDICINE. ORO-125.

Edited by Gould A. Andrews, Marshall Brucer, and E. B. Anderson. United States Government Printing Office, Washington, D. C., 1955. 817 pp.

The following chapters are those contributed to this book by members of the staff of the Medical Division:

Chapter 3. SOME ASPECTS OF THE PATHOLOGY OF RADIATION. Ralph M. Kniseley.* pp. 35-44.

Chapter 5. BIOCHEMICAL CONSIDERATIONS OF DISTRIBUTION. G. C. Kyker. pp. 50-62.

Chapter 6. SOME ASPECTS OF RADIOASSAY AND INTERPRETATION. C. L. Comar. pp. 63-72.

Chapter 10. GAMMA RAY ABSORPTION AND RADIATION DOSIMETRY. Marshall Brucer. pp. 103-153.

Chapter 27. PATHOLOGIC CHANGES PRODUCED IN THE THYROID BY I-131. Ralph M. Kniseley* and Gould A. Andrews. pp. 400-411.

Chapter 38. INTRACAVITARY USE OF RADIOISOTOPES. Gould A. Andrews. pp. 552-563.

The following discussion periods were opened by members of the staff of the Medical Division:

Discussion of Chapters 7 and 8. R. L. Hayes. pp. 86-88.

Discussion of Chapter 13. Samuel W. Root.** pp. 197-198.

Discussion of Chapters 16 and 17. Marshall Brucer. pp. 236-238.

Discussion of Chapters 32 and 33. Malcolm P. Tyor.*** pp. 478-480.

Discussion of Chapter 35. Gould A. Andrews. pp. 511-512.

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***Present address:
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Durham, North Carolina

Discussion of Chapters 37, 38, and 39. Marshall Brucer. pp. 581-583.

Discussion of Chapters 40 and 41. Ralph M. Kniseley.* pp. 617-619.

The following chapters were prepared by the clinical staff of the Medical Division:

Chapter 29. CLINIC ON THYROID DISEASE. pp. 414-428.

Chapter 36. CLINIC ON BLOOD DISEASES. pp. 517-532.

Chapter 42. CLINIC ON THERAPY WITH RADIOACTIVE COLLOIDS. pp. 622-634.

ORINS HOSPITAL PATIENT-DAYS

July	434
August	421
September	309
October	359
November	339
December	273
January	408
February	403
March	439
April	304
May	559
June	535
Total patient-days	4783

RESEARCH PARTICIPANTS

Roy V. Talmage	Rice Institute
Frederick W. Lengemann	University of Tennessee
Michael K. Berkut	University of North Carolina
George T. Johnson	University of Arkansas
David B. Camp	University of the South

RESIDENT PHYSICIANS

Francisco Comas	Penrose Cancer Hospital Colorado Springs, Colorado
Fleming McConnell	Massachusetts General Hospital Boston, Massachusetts
Rodrigo Bernal	Duke University Hospital Durham, North Carolina
Zeth Gabrielsen	Tulane University New Orleans, Louisiana
Bernard T. Hickman	Ochsner Foundation Hospital New Orleans, Louisiana
Harry M. Walsh	Wayne County General Hospital Eloise, Michigan
Ivan E. Rhodes	Boston City Hospital Boston, Massachusetts
Jan Wybranowski	St. Mary's Hospital Knoxville, Tennessee
Majic Potsaid	Massachusetts General Hospital Boston, Massachusetts

NONEMPLOYEE VISITORS

Hirotake Kakehi	Faculty of Medicine Tokyo University Tokyo, Japan
Renaat Loos	University of Ghent Ghent, Belgium
Mamoon Magid	University of Cairo Cairo, Egypt
Kamal Abd Mahmoud	University of Cairo Cairo, Egypt
Jean D. Mewissen	University of Liege Liege, Belgium
Fearghus O'Foghludha	St. Luke's Hospital Dublin, Ireland
Chiyeko Okawa	St. Luke's International Hospital Tokyo, Japan
Thomas E. Shockley	Meharry Medical College Nashville, Tennessee
Kuang-Chu Wang	Taiwan University Taipei, Taiwan, Formosa

RESIDENT IN EXPERIMENTAL MEDICINE

Robert B. Sudrann	Private Practice Seattle, Washington

POSTRESIDENT STAFF MEMBERS

Carlyne Newman	City Hospital Cleveland, Ohio
Francisco Comas	Penrose Cancer Hospital Colorado Springs, Colorado

MILITARY PERSONNEL

John C. Schooley	US Army
Herbert Lennox	US Navy

MEDICAL EVALUATION COMMITTEE

Carl V. Moore, chairman	School of Medicine Washington University
Joseph C. Bell	School of Medicine University of Louisville
Horace Davenport	College of Medicine University of Utah
Frank W. Putnam	College of Medicine University of Florida
Carl F. Tessmer	Armed Forces Institute of Pathology

*Present address:
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Eden Hospital
Castro Valley, California

6/30/57

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Eleventh Annual Report

of the

Oak Ridge Institute of Nuclear Studies

OPERATING UNDER CONTRACT

with the

United States Atomic Energy Commission

JUNE 30, 1957

Medical Division

PROBABLY never before in its history have the activities of the Medical Division had such a cosmopolitan air as during the past fiscal year. The roster of the division for 1956-57 reads like a cross section of a United Nations directory: Bellenghi and Manaresi, Italy; Faust, Berger, Huppe, and Winkler, Germany; Comas, Spain; Fujita, Kakehi, and Kanno, Japan; Loos and Mewissen, Belgium; Sivaramakrishnan, India; Papadopoulou and Samaras, Greece; Ullberg, Sweden; O'Foghludha, Ireland; Wang, Formosa; Oddie, Australia; Stephens, St. Aubin, Skorey, Momose, and Vezina, Canada; Otero-Ruiz, Colombia—all played active roles in Medical Division activities during the year just passed.

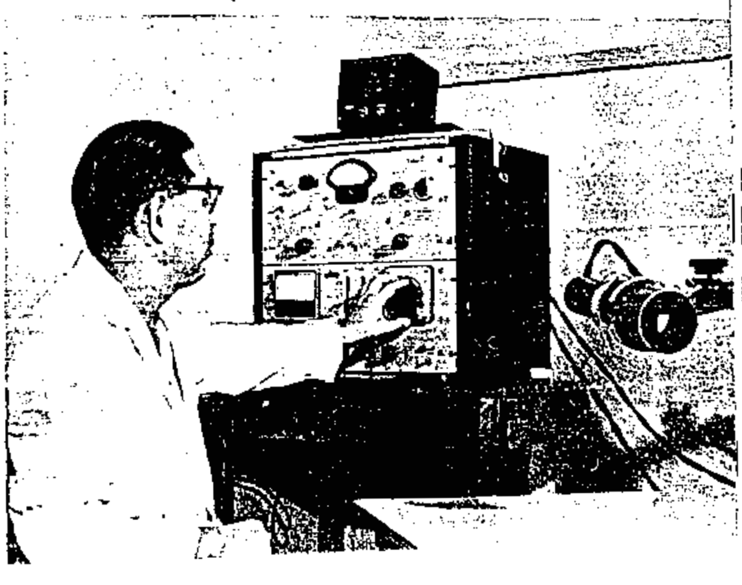
Conversely, regular division staff members were more involved than ever before in scientific meetings on an international scale. Division chairman Marshall Brucer visited Japan, Formosa, the Philippines, and Mexico; Cyril L. Comar, chief of biomedical research, attended a meeting of a UNESCO consultant group in Paris; Gould A. Andrews, chief of clinical services, and visiting scientist John H. Rust, U. S. Army Veterinary Corps, were featured speakers at the Tenth Oak Ridge Regional Symposium held in Puerto Rico; and Dr. Andrews and Herbert D. Kerman, consultant to the division, were speakers at the Inter-American Symposium on the Peaceful Applications of Nuclear Energy, held at Brookhaven National Laboratory in May.

Still in the international mood was a seminar on supervoltage and gamma-ray therapy held at the Medical Division in July 1956, which was attended by some 70 radiotherapists and physicists from the United States, England, Ireland, Sweden, France, Belgium, New Zealand, Holland, China, and Japan. The meeting was a summary of the opinions of a large segment of radiotherapists on the problems of supervoltage therapy, and the proceedings will be published in the early part of 1958.

In addition, the division acted as host to a group of medical participants at the Brookhaven Inter-American Symposium; a special program was presented by the division when the foreign scientists visited Oak Ridge.

In the course of the year, too, scores of citizens from many foreign countries visited the Medical Division. Hiroshi Maki, a coordinator for the Atomic Bomb Casualty Commission in Japan, for example, took a two-week indoctrination in radioactivity-measurement techniques under Hirotake Kakehi in January and February. J. E. Roberts, of the Middlesex Hospital, London, and editor of "Physics in Biology and Medicine," was the representative of the English surveyees at the third thyroid-uptake seminar, held in March. And R. C. Vickery, formerly of the University of Melbourne, now head of the Department of Chemistry at Horizons, Inc., in Cleveland, and an international authority on rare earths, presented the division with a gram of lutecium oxide after a discussion with Granvil C. Kyker, chief of laboratory research, concerning the division's rare-earth program.

Junichi Fujita, visiting scientist from Tokyo, Japan, works with a double collimator system to make the isoresponse curves necessary to design the heads for the ORINS profile scanner.



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NATIONAL MEETINGS AND CONFERENCES

Members of the Medical Division staff continued to take an active part in national meetings and conferences during the year. Dr. Kyker, for instance, attended a meeting of the Atomic Energy Commission Biomedical Directors in Washington, D. C., September 27-29, and Dr. Brucer attended another, April 29-30. In October, Dr. Brucer attended a meeting of the Committee to Study the Use of Radioactive Isotopes and Other Materials and to Report to the Board of Trustees at the Next Clinical Meeting of the American Medical Association.

In April, also, three members of the Medical Division staff appeared on the program of the meetings of the Federation of American Societies for Experimental Biology, held in Chicago. Dr. Comar took part in an April meeting of a special group called together at the request of Charles L. Dunham, director of the AEC Division of Biology and Medicine, Washington, D. C., to study the deposition and retention of strontium-90 in the skeleton. (Dr. Comar, incidentally, is senior editor of a forthcoming book published by the Academic press, "Mineral Metabolism: An Advanced Treatise.")

To round out the fiscal year, Drs. Brucer, Ross, Kakehi, Andrews, Kyker, and Hayes conducted a course in thyroid radioiodine-uptake measurement at the meeting of the Society of Nuclear Medicine, held in Oklahoma City June 20-22. A Medical Division exhibit on "midget exhibits" was also shown at the meeting of the Society, of which Dr. Brucer is president-elect and Drs. Andrews and Kyker are on its board of directors. Dr. Kyker is also chairman for the 1958 meeting of the society.

The foregoing are but highlights; staff members of the division took part in many smaller meetings, conferences, and consultations in all parts of the country.

THYROID-UPTAKE CALIBRATION PROGRAM

During the year, the Medical Division completed the first and second phases of its thyroid-uptake calibration program, begun in 1953, and was well on its way through the third phase. The object of the program is to standardize methods for measuring the uptake of radioactive iodine by the thyroid gland, in order to achieve accurate results regardless of the various combinations of measuring equipment used. The first stage involved sending half-body manikins with artificial thyroids containing an iodine substitute to scientists throughout the country and several European countries, for measurement by various methods. In the second stage, the many hundreds of results obtained were compared and analyzed, and after months of study and work, a standard system of calibration was arrived at. The third phase, that of imparting this system to the persons most concerned with its use, was begun in September 1956. In that month, the first of a series of seminars was given at the Medical Division's training wing. This initial seminar was attended by 16 prominent experts in the field, and the ensuing series was based on experience gleaned from the first. It was decided to present the seminars to about six groups: two groups of physicians and physicists who participated in the original survey, two groups of other qualified physicians and physicists, one group of representatives of American manufacturers of thyroid-uptake equipment, and one group of technicians employed by the persons who participated in the seminar.

A rotating chair used to match multipositional [illegible]roid-uptake studies.

Six of these seminars were presented during the fiscal year, with an additional one spe-

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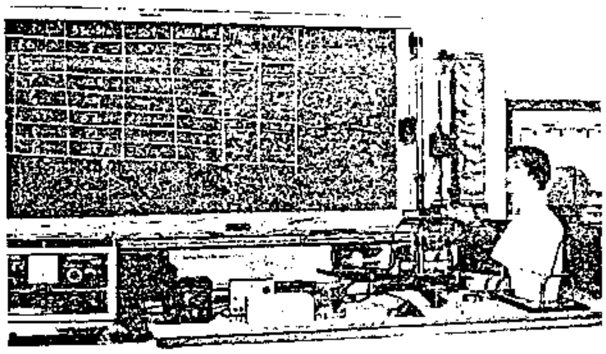
cifically directed towards technicians planned for August 1957. According to a report by the Medical Division, the success of these seminars and of the whole thyroid-uptake calibration program is attested to by the stimulated interest in repetition of experiments concerning the accuracy of thyroid-uptake measurements. At the meeting of the Society of Nuclear Medicine mentioned previously, a number of papers were presented on the accuracy of these calibrations, and a number of papers have appeared in the literature verifying or criticizing the Medical Division's techniques. Many manufacturers are redesigning their equipment to meet the objections pointed out in the thyroid-uptake-calibration survey. A further evidence of the interest in this program is the fact that three manikins will be sent to England, Japan, and Australia for survey purposes early in 1958.



A demonstration setup is used in the training seminars to show the significance of each experiment before the participants conduct the experiment themselves.

SCANNING PROGRAMS

One of the most formidable difficulties encountered in scanning a patient's body for concentration of previously administered radioactive material is the variation in depth at which the material may lie. A detecting device, or scanner, is inherently more sensitive to nearby emitters; as a consequence, the picture provided by the scanner is a distorted one, unless some method is used to equalize, or at least roughly level off, its response at all depths concerned. Such compensation methods in turn produce new problems—for example, variable sharpness of focus—and it is by no means certain that the Medical Division's current scanning detectors represent a judicious compro-

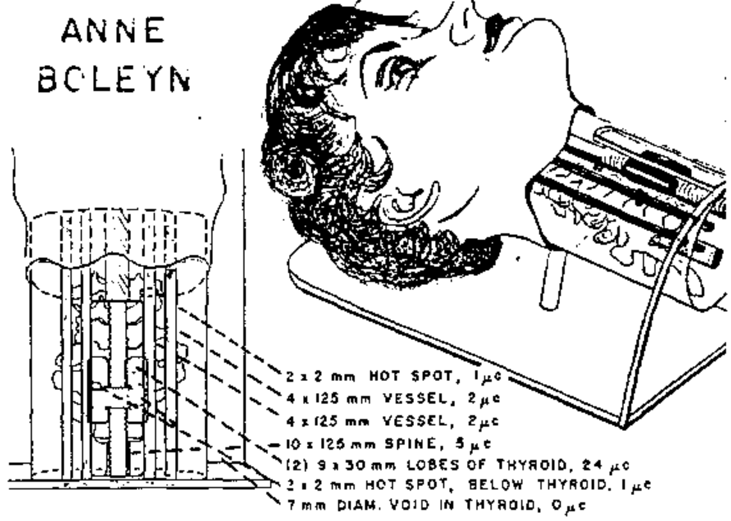
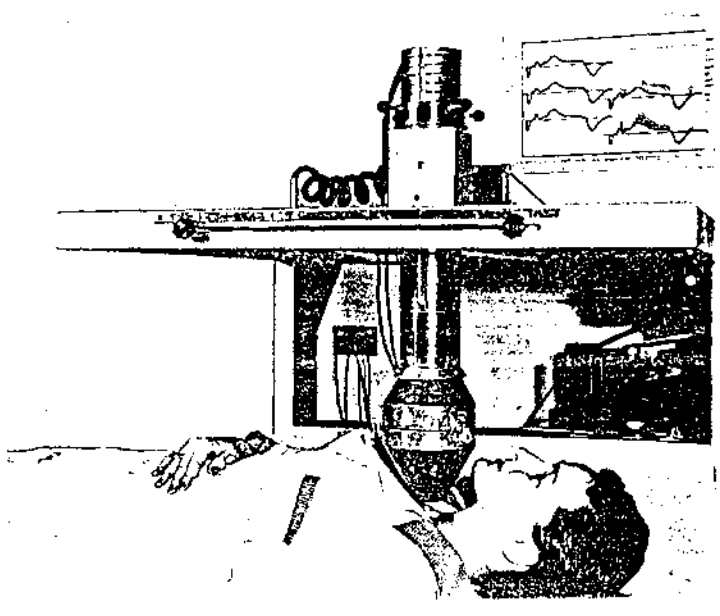


Diagram of Anne Boleyn, the head manikin, used for special scanning studies.

mise between the conflicting requirements. Accordingly, a theoretical study is in progress to ascertain whether increased crystal size and aperture number may enhance a scanner's effectiveness enough to justify the concomitant increase in cost, weight, and bulk. Above a certain point, for instance, size alone will compromise the usefulness of a scanner's detecting head.

Another difficulty in scanning is that of quantitating the scanning results. Much of the desirability of scanning is based on subjective interpretations of a pattern of marks on a piece of paper; the only way in which this subjective interpretation can be tested is to prepare a manikin for which the correct answer is known. Two such manikins, named Anne Boleyn and Bonnie Boleyn, have been prepared and will be taken for testing in the near future to various laboratories active in the scanning program. The Medical Division is also preparing a hand-

After calibration with the Anne (or Bonnie) Boleyn manikin, the scanner is used in studies with patients.



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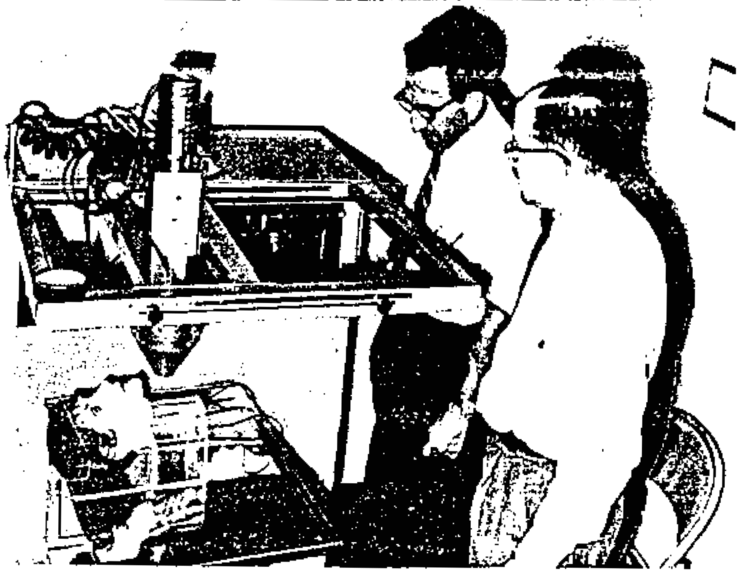


A. Stone Freedberg, of Harvard Medical School and the Beth Israel Hospital in Boston, and Gerald Hine from the Boston VA Hospital are among the many experts who have reviewed the scanning studies at the Medical Division.

book of scanning procedures for publication as an ORINS document by the Technical Information Services Extension of the Atomic Energy Commission.

A great deal of work has been done by the Medical Division on localized scanning problems such as delineating the size, shape, and position of the thyroid gland. Other areas of the body, such as the liver and kidneys, have been investigated, but the scanning requirements are not so clear-cut in these regions. As a part of the larger field of external localization, the Medical Division is following a technique announced by Professor Eric Pochin, of London, England, several years ago. This technique is called "profile scanning."

In this adaptation of the external scanning procedure, the counting device moves across the total length of the patient and measures a thin slit of activity in one cross-sectional area. One of the advantages to be expected from the profile scanner is an estimate of total-body activity; however, this has a lower research priority than strip-scanning through the length of the body.

Harry Kimble, senior instrument maker with the ORINS Technical Shops, is now working on this latter type of device, using a battery of six scanners that will traverse the patient's length. The design is based on preliminary isoresponse curves prepared by Junichi Fujita, of the Second National Hospital in Tokyo, a visiting scientist working at the Medical Division.

At the end of the year Douglas A. Ross, chief of medical physics, and instrument engineer A. C. Morris, Jr., with the help of an Oak Ridge National Laboratory team headed by P. R. Bell, J. E. Francis, and C. C. Harris, are building a device that will accomplish the profile scanning in a manner more specifically directed toward clinical problems. In pulmonary investigations, for instance, a patient may inhale a radioactive gas (xenon, for example, or an iodine-carrying substance), and a large number of strategically placed sensing heads record counts for different segments of the pulmonary cavity. This method can also be used by injecting radioactive material into the patient and charting its distribution to the lung.

The main problem here is to get 20 or more sensing heads spaced properly, each "looking" at some section of the lung, not interfering with other recorders, and all operating efficiently. A fast-reading device to follow individual inhalations and exhalations is also a necessity. Dr. Ross and Mr. Morris plan to start with a one-channel analyzer and, when it is working successfully, go on and add other channels until the desired design is attained.

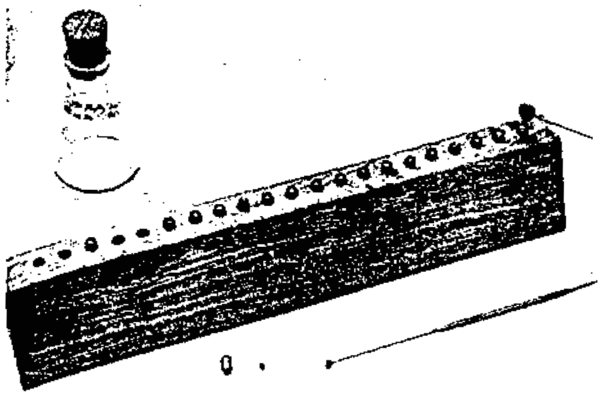
BRACHYTHERAPY PROGRAM

Approximately 700 cobalt-60 brachytherapy beads made of Incoray alloy (International Nickel Company) have been distributed to some fifteen radiotherapists throughout the country. The very small (1-millimeter-diameter) point-source beads were irradiated in the Oak Ridge reactor for one year to attain an activity of approximately 1 millicurie per bead. Most of these beads will be used by Carl Tessmer in the Armed Forces Institute of Pathology on radiobiological studies. However, they do have an immediate practical use and will be sent to a number of radiotherapists for clinical testing.

A number of uterine applicators have been manufactured, but the problems of loading, sealing, and calibrating the devices have not yet been solved. The applicators are being made specifically for Norman Simon's group at Mount Sinai Hospital in New York City.

Europium-152 beads were made specifically from a design of Paul St. Aubin at the Massachusetts General Hospital. The calibration of time necessary for irradiation to required specific activities has been determined, and these beads will be manufactured in quantities necessary for therapeutic tests next year.

A number of cobalt-60 Incoray needles have been manufactured and are ready for distribution to radiotherapists for clinical tests. No further devices that are being matched in other laboratories or are commercially available will be manufactured on this program.



After spending considerable time designing complex loading machinery, the Medical Division reverted to the simplest method of loading stable europium into brachytherapy beads. The powder is dipped with a small measuring cup and poured through a small funnel into the bead. A small screw holds the powder in place and a drop of solder over the screw seals the source.

RARE EARTH PROGRAM

During the past year, there has been some reduction in experimental effort of the division's rare-earth program and increased time has been devoted to evaluation of results and preparation of reports. One report is in press, another is submitted, and a number of others are in progress.

Michael K. Berkut, research participant from the University of North Carolina School of Chemistry, has continued autoradiographic studies with potassium, rubidium, and calcium in relation to calcification of the bone. The summer of 1957 has been devoted largely to analysis, interpretation, and laboratory work on reports. At the year's end, one report was submitted for publication and others were in preparation.

One of the major problem areas in the internal use of isotopes includes the very complex changes in metabolism that accompany the growth of cancer. It is becoming less instructive to follow the course of internal isotopes without simultaneously following the metabolic changes that occur. Arthur L. Kretchmar is setting up in the clinical laboratories a metabolic unit that will allow the same kind of controlled studies in the human patient that are now done in experimental animals.

One of the first of his studies has been to investigate the effects of ACTH in protein metabolism. One report in this field will be published in the near future, and another is in the manuscript-typing stage.

V. M. Sivaramakrishnan, Fulbright exchange student, has made a significant contribution to studies of the effect of injury to the liver caused by intravenous rare-earth injection. A report on Dr. Sivaramakrishnan's work was made to the Federation of American Societies for Experimental Biology in April 1957. Since that time, Dr. Sivaramakrishnan has been continuing his work in this field, with particular reference to the use of various other metals as possible protection against this injury.

In connection with this same investigation of injury to the liver, the Medical Division has been fortunate to enlist the services of Carl Lee Anderson of the University of North Carolina. Dr. Anderson, as collaborator, is carrying out special analyses of some special fractions of liver fats, from livers sent him by the division.

Another important collaborative program is that being carried out with the assistance of W. M. Christopherson of the University of Louisville Department of Pathology. This program involves the intramammary administration of lutecium in dogs, in different chemical preparations, for study of its comparative effectiveness of selective lymphatic radiation. In general, these have included organic preparations (low-carrier and high-carrier), citrate complexes, and serum-protein complexes. To date, citrate appears superior to other substances in its selective lymphatic localization. In the cooperative program, the Medical Division designs and produces the different chemical preparations, and Dr. Christopherson's group administers them and examines the tissue sections. Interpretation of results to date is now in progress, but there is as yet no clinical confirmation or the opportunity to carry out the same work in humans.

PATHOLOGY

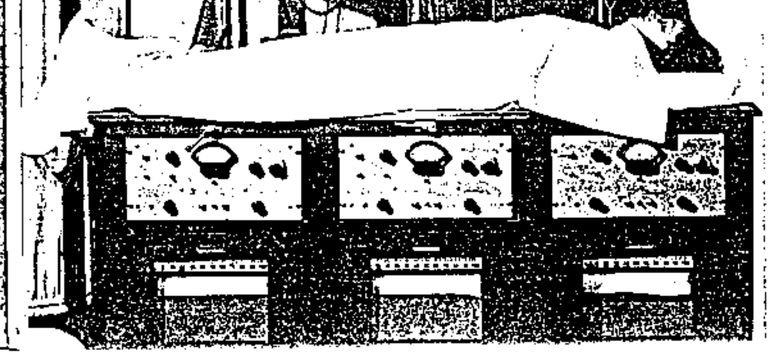
A one-year program for pathology residents in the Medical Division has been established, and approved by the American Medical Association. Residents, however, may be accepted for periods as short as four months. The pathology residents will receive training primarily in the clinical diagnostic uses of isotopes. The first resident under this program, William D. Huffines of the University of North Carolina School of Medicine, arrived on April 28, 1957.

Staff members have conducted all the pathological studies in the division's rare-earth program, and have studied sections of intestinal tracts in connection with the Armed Forces Special Weapons contract.

Techniques for quantitation of gross autoradiograms have been worked on during this period. The major difficulty encountered has been the lack of linear correlation between film response and the intensity of radiation, except over relatively narrow limits. If these limits are observed, good quantitation can be obtained.

Staff members C. Harold Steffee and Joe Gray received additional training during the year at the Ortho Research Institute, Raritan, New Jersey, in techniques for determining minor blood types. There are over 50,000 possible blood-type combinations known. By following many possible factors, the division is attempting to determine whether or not bone-marrow transplants given to patients who have received total-body irradiation will survive.

Triple spectrometer used in thyroid-uptake studies.



CLINICAL STUDIES

Studies relating to total-body irradiation and bone-marrow transplantation have been of considerable interest during the year, and many important data have been derived from these studies. Techniques for separating human marrow from healthy donors and reinjecting it into patients have been worked out, and appear to be satisfactory. It is hoped that marrow transplantation can be used as a treatment for radiation accidents, and might also be used as a form of therapy for certain diseases where the normal marrow has been greatly depressed or destroyed by large doses of radiation or marrow-damaging drugs. Certain long-range problems having to do with the survival of transplanted marrow and possible therapeutic uses were being set up at the close of the fiscal year.

Continuing studies of the scintiscanner in clinical work have helped to delineate its values and limitations. Correlations with surgical specimens and autoradiograms have been possible in a considerable number of patients, especially those with thyroid diseases. The training program has continued to expand, and has included a considerable number of noncitizen scientists.

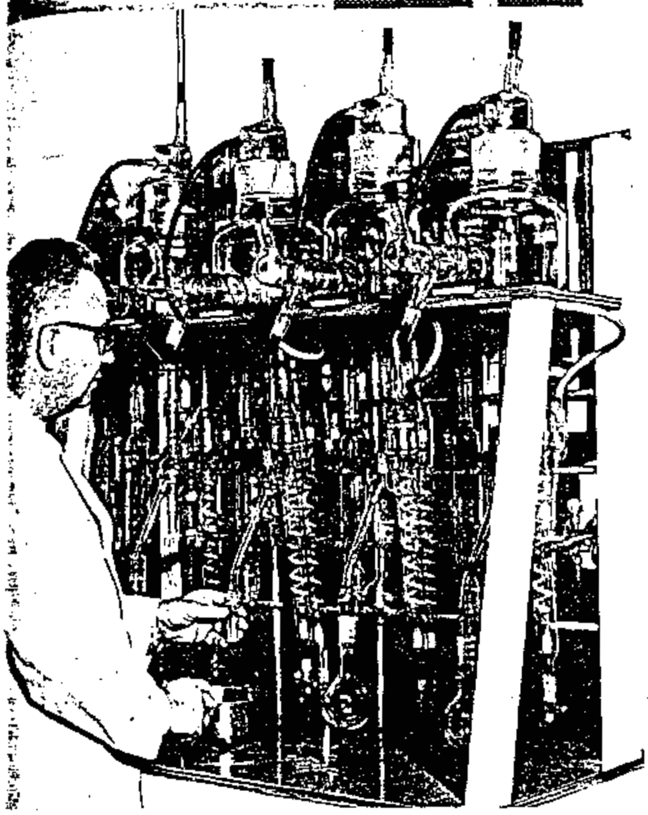
The division is continuing its studies on radioactive colloids, evaluating the use of gold-198, yttrium-90, and lutecium-177 in various clinical situations.

A considerable number of patients with polycythemia vera have been treated for several years by the Medical Division. A few of these patients are now developing mylofibrosis, and the red-cell dynamics are being studied in these patients.

Closely related to the foregoing is a study of the use of phosphorus-32 in various diseases. The division has a considerable volume of assay and autoradiographic data, which is being assessed and evaluated and will be reported on in the near future.

THYROID-COLLECTION PROGRAM

The division's thyroid-collection program has been continued during the year, and the



Col. John H. Rust studies the metabolism of carbon-14 in rats.

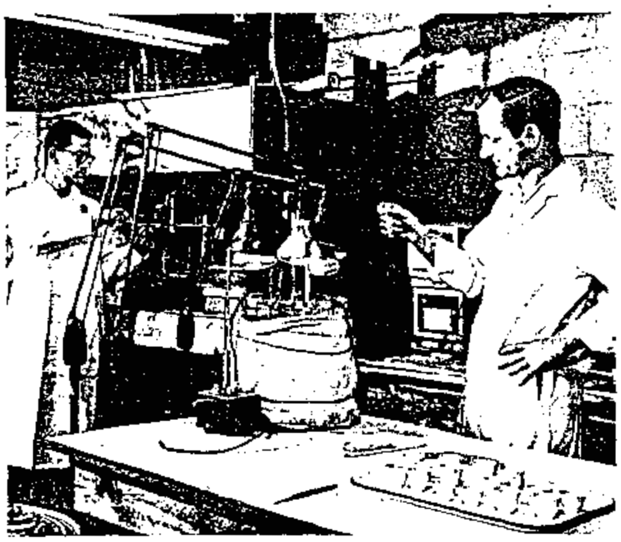
ıdings to date have been accepted for publication in the July 5, 1957, issue of "Science." The main points, as summarized in the article, are these: The Medical Division has assembled data on a two-year base period, and has been able to evaluate the effects of nuclear weapons tests by various countries. Human and animal glands from all over the country have been analyzed by the division for radioiodine content. By making comparisons with the observed levels and with the amounts that have been known to cause observable effects, it has been concluded that the levels of radioactive iodine constitute no hazard.

BIOMEDICAL RESEARCH

Work on the measurement of radiation dosage to the intestinal tract from radioactive materials passing through the tract has been continued under the Armed Forces Special Weapons contract. Studies have been completed on large numbers of dogs and goats, and the physical and biological techniques have been worked out to the point where they are entirely satisfactory for the purpose. Results are now available as to the part of the gastrointestinal ·act receiving the highest dosage and the actual dosages received in terms of the amounts ingested. The effects of important factors such as conditions of constipation and diarrhea have been evaluated. Parameters such as amounts of food ingested, rate of passage through the gastrointestinal tract, the geometry of the gastrointestinal tract, and the changes in concentration during passage have been investigated to permit extrapolation to man.

Because of the general interest and importance of the subject, the Medical Division has carried out an extensive experimental program of study on the comparative metabolism of calcium and strontium in both animals and man. On the basis of these studies, predictions of the strontium level in the human population can be made when the amounts falling upon the surface of the earth are either known or can be predicted. The investigation of the metabolism of strontium has led to the consideration of approaches whereby the amount of strontium getting into the human population can be modified. A series of conferences on the problem were held between division staff members and government officials carrying responsibility in these matters.

In the course of the year, a series of studies were made on the metabolism of 1-carbon fragments, utilizing carbon-14 techniques. These studies were completed early in 1957. Research



Senior scientist Robert Wasserman and F. W. Lengemann, research participant from the University of Tennessee, conducting biomedical research in the animal laboratories.

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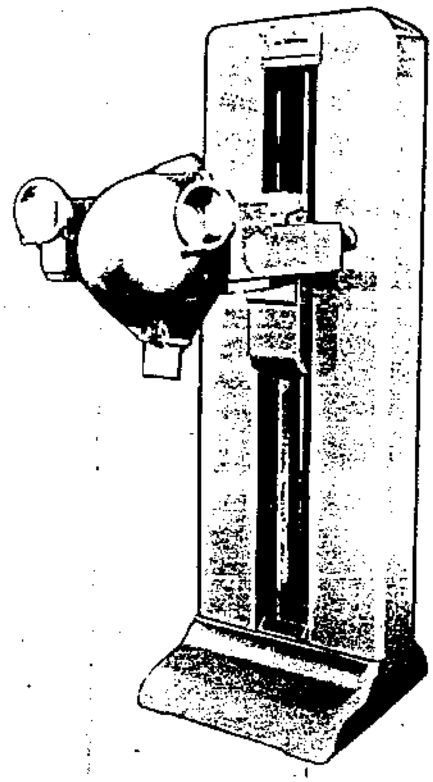
is now in progress to determine the source of carbon in urea. So far, it has been determined that it does not derive from the plasma carbon-dioxide pool; probably, it comes from one of the carbons in glucose. The source has not yet been identified, but work is continuing, and it is hoped that more definite data will be available in the near future.



APPENDIX III

Medical Division

CONSULTANTS TO THE MEDICAL DIVISION

ALABAMA

Medical College of Alabama
Champ Lyons
William H. Riser

ARKANSAS

University of Arkansas Medical Center
Howard J. Barnhard

CALIFORNIA

Cedars of Lebanon Hospital
Stanley H. Clark

City of Hope Medical Center
Melville L. Jacobs

Eden Hospital
Ralph M. Kniseley

Los Angeles Veterans Administration Center
Franz K. Bauer

University of California at Los Angeles
Benedict Cassen

UCLA Medical Center
Raymond L. Libby

University of Southern California School of Medicine
Henry L. Jaffe

COLORADO

University of Colorado
Jerry K. Aikawa

DISTRICT OF COLUMBIA

AEC, Washington, D. C.
Paul C. Aebersold

FLORIDA

Florida State Board of Health
Lorenzo L. Parks

Halifax District Hospital
Herbert D. Kerman

Private Physicians
Louis M. Orr
Samuel W. Root

University of Florida
George T. Harrell
Francis C. Ray

GEORGIA

Emory University School of Medicine
Harry D. Bruner
Bryan Redd
H. Stephen Weens

University of Georgia School of Medicine
Stephen W. Brown

Medical College of Georgia
Claude-Starr Wright

ILLINOIS

Cook County Hospital
Irvin F. Hummon

KANSAS

University of Kansas
Frank E. Hoecker

University of Kansas School of Medicine
Galen M. Tice

KENTUCKY

University of Louisville School of Medicine
Harold F. Berg
William M. Christopherson
Ji-toong Ling

LOUISIANA

Ochsner Clinic
William R. Arrowsmith
Paul J. Murison

Tulane University
John U. Hidalgo
Robert T. Nieset

MARYLAND

National Institutes of Health
George Z. Williams

MASSACHUSETTS

Harvard University Medical School
A. Stone Freedberg

Massachusetts General Hospital
Paul M. St. Aubin

MICHIGAN

University of Michigan School of Medicine
Jere Bauer
Halvor N. Christensen
Adam A. Christman
M. J. Coon

Wayne County General Hospital
Lyndon E. Lee

Wayne University College of Medicine
James E. Lofstrom

MISSISSIPPI

University of Mississippi Medical Center
Arthur C. Guyton
Robert D. Sloan

MISSOURI

Private Physician
Wendell G. Scott

University of Missouri School of Medicine
Walter J. Brudette

NEBRASKA

Creighton University School of Medicine
James F. Kelly, Jr.

University of Nebraska
Howard B. Hunt
Merle M. Musselman
Arthur Tuma

NEW YORK

AEC, New York Operations Office
S. Allan Lough

Francis Delafield Hospital
Carl B. Braestrup

Hospital for Joint Diseases
Milton Friedman

New York University - Bellevue Center
Sidney Rubenfeld

Private Physician
Norman Simon

State University of New York
Paul A. Riemenschneider

Syracuse Memorial Hospital
Alfred S. Berne
G. Ferlazzo

NORTH CAROLINA

Bowman Gray School of Medicine
Camillo Artom
Isadore Meschan

Duke University School of Medicine
William G. Anlyan
Wilburt C. Davison
William P. Deiss
Philip Handler
Jerome S. Harris
Harold W. Lewis
Robert J. Reeves
C. R. Stevens
Malcolm P. Tyor

University of North Carolina
John H. Ferguson
Charles D. Van Cleave

NORTH DAKOTA

University of North Dakota School of Medicine
William E. Cornatzer

OREGON

University of Oregon Medical School
Carl Hopkins

PENNSYLVANIA

Temple University School of Medicine
R. C. Baldridge

SOUTH CAROLINA

Medical College of the State of South Carolina
John C. Hawk

TENNESSEE

Carson Newman College
Carl T. Bahner

Oak Ridge Hospital
Robert P. Ball
Robert R. Bigelow
Dana W. Nance
W. W. Pugh, Jr.
C. J. Speas
Paul E. Spray

University of Tennessee College of Medicine
David S. Carroll
Alfred P. Kraus
Carl E. Nurnberger
Jesse D. Perkinson, Jr.
John L. Wood
Robert A. Woodbury

Vanderbilt University
Herbert Francis
Granville Hudson
C. C. McClure

Veterans Administration Hospital
George R. Meneely

TEXAS

M. D. Anderson Hospital
Gilbert H. Fletcher
Robert J. Shalek

Baylor University
Vincent Collins
Harold Tivey

Brooke Army Medical Center
J. A. Isherwood

University of Texas Medical Branch
Ludwik Anigstein
Robert N. Cooley
Wendell D. Gingrich
William C. Levin
Wiktor W. Nowinski
Martin Schneider
Vernie A. Stembridge
Howard G. Swann

VIRGINIA

Medical College of Virginia
Frederick B. Mandeville

University of Virginia
George Cooper
Kenneth R. Crispell
George R. Minor

WISCONSIN

University of Wisconsin
Edgar S. Gordon

PUERTO RICO

University of Puerto Rico
Conrado Asenjo

THYROID UPTAKE CALIBRATION SEMINAR SERIES

EXPERIMENTAL SEMINAR TU - cy
September 24-28, 1956

David Becker	New York Hospital New York City
Benedict Cassen	University of California West Los Angeles, California
Theodore Fields	VA Hospital Chicago, Illinois
A. Stone Freedberg	Harvard University Boston, Massachusetts
Edgar S. Gordon	University of Wisconsin Madison, Wisconsin
Otto Hanson	Santa Fe Railway Hospital Topeka, Kansas

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ohn U. Hidalgo	Tulane University New Orleans, Louisiana
Gerald Hine	Boston VA Hospital Boston, Massachusetts
Frank E. Hoecker	University of Kansas Lawrence, Kansas
Jesse E. Hoffman	Veterans Administration Nashville, Tennessee
H. D. Kerman	Halifax District Hospital Daytona Beach, Florida
S. Allan Lough	City of New York Hospitals New York City
George R. Meneely	Vanderbilt University Nashville, Tennessee
Lindon Seed	Prudential Plaza Chicago, Illinois
Bob Schulz	Memorial Hospital New York City
Robert E. Zipf	Miami Valley Hospital Dayton, Ohio

SEMINAR A
January 14-15, 1957 TU-A

G. W. Buckaloo	VA Hospital Kansas City, Missouri
W. H. Cargill	VA Hospital Atlanta, Georgia
S. F. Crabtree	Maxwell Air Force Base Alabama
John Foster	DePaul Hospital Norfolk, Virginia
. J. Henderson	West Side VA Hospital Chicago, Illinois
Justin Huppe	Massachusetts General Hospital Boston, Massachusetts
P. C. Johnson	VA Hospital Oklahoma City, Oklahoma
Norman D. Lee	VA Medical Teaching Group Hospital Memphis, Tennessee
B. H. McCraw	VA Hospital Durham, North Carolina
W. B. Miller	Central Isotope Laboratory Emory University, Georgia
S. Paul Perry	Watts Hospital Durham, North Carolina
R. E. Peterson	State University of Iowa Iowa City, Iowa
Louis Raider	Providence Hospital Mobile, Alabama
W. H. Sprunt, III	Medical School University of North Carolina Chapel Hill, North Carolina
W. C. A. Sternbergh	Charlotte Memorial Hospital Charlotte, North Carolina
Sol Taplits	Jewish Hospital Cincinnati, Ohio

SEMINAR B
February 11-12, 1957 TU-B

Jen Hung Chao	Mercy Hospital Institute of Radiation Therapy Chicago, Illinois
Carl H. Clark	Alabama Polytechnic Institute Auburn, Alabama
D. B. Darling	ORINS Medical Division Oak Ridge, Tennessee
T. P. DePalo	Milford Medical Clinic Milford, Massachusetts
W. F. Dowling	St. Elizabeth's Hospital Boston, Massachusetts
E. Frank Dunton	John Sealy Hospital Galveston, Texas
Josef Enzinger	Bird S. Coler Hospital New York City
D. V. Foley	Mercy Hospital Institute of Radiation Therapy Chicago, Illinois
D. C. Gastineau	Indiana University Medical Center Indianapolis, Indiana
W. A. Griesbach	Cincinnati General Hospital Cincinnati, Ohio
W. L. Hawley	VA Hospital Birmingham, Alabama
I. F. Hummon	Cook County Hospital Chicago, Illinois
Melville L. Jacobs	City of Hope National Medical Center Duarte, California
Iwao Kanno	Tohuku University Sendai, Japan
J. C. Katterjohn	Walter Reed Army Hospital Washington, D. C.
C. T. Knorpp	VA Hospital Ann Arbor, Michigan
R. S. Landauer	Cook County Hospital Chicago, Illinois
S. H. Macht	Washington County Hospital Hagerstown, Maryland
Daphne Papadopoulou	Greek Anticancer Institute Athens, Greece
R. S. Richards	Massachusetts General Hospital Boston, Massachusetts
Joseph Rivera	Queens General Hospital Jamaica, New York
E. L. Saenger	General Hospital Cincinnati, Ohio
Vrysiis Samara	Maleytirion Alexander Hospital Athens, Greece
A. F. Spear, Jr.	VA Hospital Birmingham, Alabama
S. G. F. Ullberg	Royal Veterinary College Stockholm, Sweden
I. B. Vyas	Abbott and Janney Children's Hospital Minneapolis, Minnesota

SEMINAR 1
March 18-19, 1957 TU-1

Hubert E. Batten	Cape Fear Valley Hospital Fayetteville, North Carolina
J. H. Bowen	Blount Memorial Hospital Maryville, Tennessee

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Edward K. Carter	Holston Valley Community Hospital Kingsport, Tennessee
Waldo D. DeVore	Nuclear Consultants, Inc. St. Louis, Missouri
James B. Ely	University of Tennessee Knoxville, Tennessee
Hans H. Faust	Baptist Hospital Knoxville, Tennessee
William Harrison, Jr.	Holston Valley Community Hospital Kingsport, Tennessee
J. W. Lewis	Colorado Springs Medical Center Colorado Springs, Colorado
T. G. Mitchell	US Naval Hospital Bethesda, Maryland
J. Eric Roberts	Barnato Joel Laboratories Middlesex Hospital London, England
G. W. Schlaseman	Watts Hospital Durham, North Carolina
Orson P. Smith	Kentucky Baptist Hospital Louisville, Kentucky
Harold Swanberg	Mississippi Valley Medical Journal Qunicy, Illinois
J. A. Vezina	Laval University Quebec, Canada
Cuno Winkler	Universitats-Klinick Bonn, Germany

SEMINAR 2
April 15-16, 1957

TU-2

Charles A. Bream	University of North Carolina Chapel Hill, North Carolina
J. J. Cancelmo, Jr.	Coatesville Hospital Coatesville, Pennsylvania
W. S. Dingledine	University of Michigan Hospital Ann Arbor, Michigan
E. M. Edington	Private Practice Knoxville, Tennessee
Junichi Fujita	Second National Hospital of Tokyo Tokyo, Japan
O. W. Hyman, Jr.	St. Mary's Hospital Knoxville, Tennessee
Jospeh K. Isley, Jr.	Duke University Hospital Durham, North Carolina
W. R. Konneker	Nuclear Consultants, Inc. St. Louis, Missouri
G. H. Lambert	Gould Medical Group Modesto, California
H. G. Langford	University of Mississippi Medical Center Jackson, Mississippi
Frank C. Larson	University of Wisconsin Madison, Wisconsin
Julian S. Lewis	Cleveland City Hospital Cleveland, Ohio
M. Price Margolies	Coatesville Hospital Coatesville, Pennsylvania
Charles V. Miller	Erlanger Hospital Chattanooga, Tennessee
Jack M. Morgan	Eugene Talmadge Memorial Hospital Augusta, Georgia
Maurice Nataro	VA Hospital Louisville, Kentucky
Paul R. Noble	Mercy Hospital Pittsburgh, Pennsylvania
Leo Oliner	US Naval Hospital Chelsea, Massachusetts
David H. Patten	University of Maryland Hospital Baltimore, Maryland
G. T. Proctor	Blount Memorial Hospital Maryville, Tennessee
Harvey T. Pullen	Coatesville Hospital Coatesville, Pennsylvania
Cliff Ratliff, Jr.	St. Agnes Hospital Baltimore, Maryland
Paul J. Rosenbaum	Yale University School of Medicine New Haven, Connecticut
Aaron P. Sanders	Duke University Hospital Durham, North Carolina
E. E. Schwartz	Oak Ridge National Laboratory Oak Ridge, Tennessee
John F. Sherrill, Jr.	Watts Hospital Durham, North Carolina
Ernest H. Wood	University of North Carolina Chapel Hill, North Carolina
J. B. Workman	University of Maryland Hospital Baltimore, Maryland
Ralph Worsnop	Jefferson Medical College Philadelphia, Pennsylvania

SEMINAR 3
May 13, 1957

TU 3

Wendell H. Bradley	Nuclear Measurements Corp. Indianapolis, Indiana
R. R. Buntaine	Nuclear Corporation of America St. Louis, Missouri
Larry Curtis	American Electronics, Inc. Los Angeles, California
G. I. Gleason	Abbott Laboratories Oak Ridge, Tennessee
W. F. Goodyear	Tracerlab, Inc. Waltham, Massachusetts
Hugh M. Griffin	Borg-Warner Corporation Santa Ana, California
W. A. McCarthy	Victoreen Instrument Company Cleveland, Ohio
J. A. Reynolds	Picker X-Ray Corporation White Plains, New York
James C. Searles	Abbott Laboratories Orange, Connecticut
M. E. Shepherd	Nuclear-Chicago Corporation Silver Spring, Maryland
James B. Stickney	Picker X-Ray Corporation Cleveland, Ohio
William Telkamp	Borg-Warner Corporation Santa Ana, California

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S HOSPITAL PATIENT DAYS

July	544
August	535
September	520
October	524
November	512
December	322
January	373
February	424
March	481
April	545
May	517
June	544
Total patient-days	5841
Average per month	486
Average per day	16.0

PARTICIPANTS IN LOW-LEVEL COUNTING THYROID COLLECTION PROGRAM

Nicholas J. Chetta	Orleans Parish New Orleans, Louisiana
John H. Childers	University of Texas Austin, Texas
T. H. Cochran	University of Utah Salt Lake City, Utah
J. R. Dawson, Jr.	University of Minnesota Minneapolis, Minnesota
[illegible]id Freiman	Beth Israel Hospital Boston, Massachusetts
N. B. Friedman	Cedars of Lebanon Hospital Los Angeles, California
Marvin Kuschner	Bellevue Hospital Center New York, New York
K. P. McConnell	Veterans Administration Hospital Louisville, Kentucky
Hans Popper	Cook County Hospital Chicago, Illinois
Vinton D. Sneeden	Emanuel Hospital Portland, Oregon

ISOTOPES USED BY THE MEDICAL DIVISION

Isotope	mc
Antimony-124	1
Calcium-45	30
Chromium-51	4
Rachromate	11
Cerium praseodymium-144	11
Cesium barium-137	1
Cobalt-58	1
Cobalt-60	1
Cobalt alloy	1097
Europium powder	60
Gold-198	2855
Indium-114	1
Iodine-131	1847
Oriodide	387
Sodium iodide	65
Radiocaps	8.97
Risa	13
Rose bengal	19
Iridium-192	1
Iron-59	2.6
Lutecium-177	801
Mercury-203	2
Phosphorus-32	250
Potassium-42	5
Rubidium-86	10
Ruthenium-103	1
Scandium-46	1
Strontium-85	4
Strontium-89	232
Strontium-124	1
Sulfur-35	14
Yttrium-90	1801.4
Yttrium-91	30
Zinc-65	1

RESIDENT PHYSICIANS

Roy J. Barry	Massachusetts General Hospital Boston, Massachusetts
Hans E. Berger	Buffalo General Hospital Buffalo, New York
E. Frank Dunton	University of Texas Galveston, Texas
Hans H. Faust	East Tennessee Baptist Hospital Knoxville, Tennessee
William D. Huffines	University of North Carolina School of Medicine Chapel Hill, North Carolina
Justin Huppe	Boston General Hospital Boston, Massachusetts
Julian S. Lewis	Cleveland City Hospital Cleveland, Ohio
K. J. Momose	Massachusetts General Hospital Boston, Massachusetts
John W. Porter	University of Nebraska Hospital Omaha, Nebraska
Robert S. Richards	Massachusetts General Hospital Boston, Massachusetts
George R. Skorey	Mercy Hospital Canton, Ohio
John A. Vezina	Laval University Quebec, Canada

POSTRESIDENT ASSISTANTS

Francisco Comas	Penrose Cancer Hospital Colorado Springs, Colorado
Donald B. Darling	Children's Medical Center Boston, Massachusetts

NONEMPLOYEE SCIENTISTS

Guido Bellenghi	Department of the Navy Rome, Italy
E. Frank Dunton	John Sealy Hospital Galveston, Texas

Junichi Fujita	Second National Hospital of Tokyo Tokyo, Japan
Hirotake Kakehi	Tokyo University Tokyo, Japan
Iwao Kanno	Tohoku University Sendai, Japan
Renaat Loos	University of Ghent Ghent, Belgium
Jean D. Mewissen	University of Liege Liege, Belgium
Walter E. Nance	Harvard Medical School Boston, Massachusetts
Fearghus O'Foghludha	St. Luke's Hospital Dublin, Ireland
Efraim Otero-Ruiz	Instituto Nacional de Cancerologia Bogota, Colombia
Daphne Papadopoulou	Greek Anticancer Institute Athens, Greece
Vrisiis Samaras	Maieytirion Alexandra Hospital Athens, Greece
V. M. Sivaramakrishnan	University of Madras Madras, India
Sven Ullberg	Royal Veterinary College Stockholm, Sweden
Kuang-Chu Wang	Taiwan University Taipei, Taiwan, Formosa
Cuno Winkler	Bonn University Bonn, Germany

TELETHERAPY EVALUATION PROGRAM

Institution	Representative on TEP
Baylor University	Vincent Collins
Creighton University	James F. Kelly, Jr.
Duke University	Robert J. Reeves
Emory University	H. Stephen Weens
Louisiana State University	Walter J. Burdette
Medical College of Virginia	Frederick B. Mandeville
New York University (Bellevue Medical Center)	Sidney Rubenfeld
State University of New York (Syracuse)	Paul Riemenschneider
University of Alabama	William H. Riser, Jr.
University of Arkansas	Howard J. Barnhard
University of Kansas	Galen M. Tice
University of Louisville	Ji-toong Ling
University of Mississippi	Robert D. Sloan
University of Nebraska	Howard B. Hunt
University of Southern California	Henry L. Jaffe
University of Tennessee	David S. Carroll
University of Texas (Medical Branch, Galveston)	Robert N. Cooley
University of Texas (M.D. Anderson Hospital	Gilbert H. Fletcher
University of Virginia	George Cooper
Vanderbilt University	Herbert C. Francis
Wake Forest College	I. Meschan
Wayne University	James E. Lofstrom

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Brucer, Marshall

RADIOISOTOPES IN THERAPY. Oak Ridge, Tennessee, Oak Ridge Institute of Nuclear Studies, Medical Division. 38 pps., July 1956.

Brucer, Marshall

STATEMENT OF DR. MARSHALL H. BRUCER, MEDICAL DIVISION, OAK RIDGE INSTITUTE OF NUCLEAR STUDIES, OAK RIDGE, TENNESSEE. Hearings before the Subcommittee on Research and Development of the Joint Committee on Atomic Energy, Congress of the United States: Second Session on Progress Report on Atomic Energy Research in Medicine, Biology, Agriculture, and Food Preservation. June 4, 5, 6, 7, and 8, 1956. Pp. 210-241. US Government Printing Office, 1956.

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Christopherson, W. M.,[3] Berg, H. F.,[4] Kyker, G. C., and Brucer, Marshall

STUDIES OF INTERSTITIAL RADIOLUTECIUM (Lu-177) IN THE DOG. Arch. Path. 62, 441-444, 1956.

Comar, C. L.

APPLICATION OF HIGH ENERGY RADIATION IN AGRICULTURE. In Proceedings of the Conference of Collaborators from Southern Agricultural Experiment Stations, March 19-21, 1956. Southern Regional Research Laboratory, 1100 Robert E. Lee Boulevard, New Orleans 19, Louisiana.

Comar, C. L.

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1. "Greenbank," Barina Crescent, Australia
2. Now with Oak Ridge National Laboratory
3. Department of Pathology, University of Louisville
4. Department of Surgery, University of Louisville

East Lansing, Michigan. US Atomic Energy Commission report TID-7512. Pp. 105-109. (For sale by Superintendent of Documents, US Government Printing Office, Washington 25, D.C., $3.00.)

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Comar, C. L.

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Harris, C. C.,[2] Bigelow, R. R.,[3] Francis, J. E.,[2] Kelley, G. G.,[2] and Bell, P. R.[2]

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1. University Clinic of Bergen, Norway
2. Oak Ridge National Laboratory
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Loos, R.[1]

INVESTIGATION OF THE COMPLEXING ACTION OF AMINO ACIDS BY MEANS OF PAPER ELECTROPHORESIS. Pp. 163-168.

Kyker, Granvil C.

THE EFFECT OF DOSE ON THE MOBILIZATION OF RARE-EARTH RADIOISOTOPES. I. ANIMAL STUDIES. Pp. 222-240.

Andrews, Gould A.

THE EFFECT OF DOSE ON THE MOBILIZATION OF RARE-EARTH RADIOISOTOPES. II. PRELIMINARY CLINICAL STUDIES. Pp. 241-258.

Hood, S. L.,[2] and Comar, C. L.

TISSUE DISTRIBUTION AND PLACENTAL TRANSFER OF YTTRIUM-91 IN RATS AND CATTLE. Pp. 280-300.

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BEHAVIOR OF RADIOACTIVE YTTRIUM IN THE BLOOD OF RUMINANTS. Pp. 301-310.

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STUDIES OF RADIOLUTECIUM IN THE MAMMARY GLAND. Pp. 332-339.

Brucer, Marshall

DOSIMETRY CALCULATIONS AND CONFERENCE SUMMARY. Pp. 436-441.

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1. University of Ghent, Belgium
2. Charles F. Kettering Foundation
3. Department of Pathology, University of Louisville
4. Department of Surgery, University of Louisville
5. University of Tennessee

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1. Bowman Gray School of Medicine.
2. "Greenbank," Barina Crescent, Australia
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6. Now with the University of Michigan

Schachinger, Lieselotte[1]

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1. Johnson Foundation for Medical Physics
2. Chemistry Department, University of Tennessee
3. Now with Oak Ridge National Laboratory
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9. Now with VA Hospital, Durham, North Carolina

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Oak Ridge Institute of Nuclear Studies

Twelfth Annual Report

OPERATING UNDER CONTRACT

WITH THE

United States Atomic Energy Commission

JUNE 30, 1958

Medical Division

NEVER a lethargic organization, the ORINS Medical Division has completed a particularly active year—in theory and in practice, at home and abroad, in the laboratory and the hospital. Programs in the germinal stage last year came to full flower, to replace or take precedence over others being brought to successful conclusion. And, of course, there were the scores of man- (and woman-) hours devoted to the intricate but routine tasks of keeping a complex organization functioning smoothly in all phases of its operation.

Much of the work of the division has been directed toward the clinical effects of significant doses of radiation on living organisms. As early as June 1955, staff members had stressed the necessity for extensive modifications of existing procedures to take care of potential radiation-accident victims. Many of the division's varied programs tie in to this particular problem.

The bone-marrow-replacement program, started shortly after 1955, is an excellent example of the type of study that is significant not only in the treament of disease but as an immediate and direct application to the treatment of radiation-accident cases. Dosimetry studies, too, have an important bearing. Much of this program is related to the level of radiation that is most probable in a serious accident, and the level at which treatment is most necessary because it is most useful. In essence, the situation is this: Where patients have been subjected to extremely high levels of radiation, there is at present no successful method of treatment known, except for palliation of incidental complications. In the range of less than 100 roentgens, there is nothing that has to be done—patients will almost invariably recover from any physical effects incidental to the exposure. But in the very important, just sublethal range, there are procedures possible for the patient by which the lethality of the dose of radiation may be considerably reduced.

In June, the Medical Division was suddenly given the task of caring for eight persons exposed to large doses of radiation. Three were dismissed within a few days when it became evident that they had received less than 100 rads. Five of these patients were in the 300 to 400 rad (radiation absorbed dose) range—the range which may or may not be lethal, in which medical care is most necessary, and about which knowledge is scarcest. Further details of the case are given later in this report; a complete interim report on the medical care of these patients is in the process of publication.

A great deal of the division's effort during the year has gone into the training program. The use of radioisotopes is now so widespread that specific radioisotope methods are being modified and adapted to innumerable types of routine hospital uses. The necessity for training physicians in the use of radioisotopes is beginning to reach urgent proportions. Because of the increasing demands on overtime for the instruction of foreign and domestic visitors at the Medical Division, its training program is undergoing changes to make it more efficient in the future.

An unusual number of publications have been produced by members of the division during the year. Some of these are necessary reports, not strictly classed as publications and not in the open literature; some are teaching materials that are distributed only to students of the division; and some are holdovers from the previous year's work.

SCANNING PROGRAM

Improvement of scanning techniques, both in performance and interpretation, is a continuous program of the division. Proper interpretation of scans has been characterized as an art, not a science, so every means of making scanning more accurate is of extreme importance to every physician using radioactivity in his work.

Routine area scans have been continuously used, particularly in patients with thyroid disease and liver metastases. Particular interest in the group of patients with thyroid remnants or areas of functioning tumor has been advanced by repeated scanning studies.

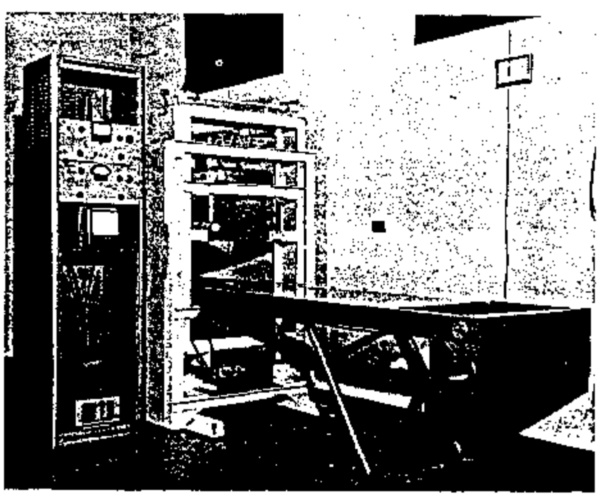
Ryosaku Tanida, resident in experimental medicine, has been carrying out a special study with a liver phantom in an effort to determine the size of nodules that can be detected by external counting techniques. This study is continuing.

It has been found that in studying patients with thyroid carcinoma previously treated by total or nearly total thyroidectomy, the use of large test doses of five or ten millicuries adds significant information over that obtained with usual tracer levels. Interest has also been shown in some special areas of activity in the teeth, salivary glands, and other areas not normally seen by scanning.

The profile scanner, which uses a battery of scanning devices to traverse the entire length of a patient, has undergone testing during the year. It has been used only to a small extent in clinical problems, but has already given promise of helping to evaluate the total distribution of radioactivity in a patient. It eliminates the great depth dependence of the area scan, and makes possible scanning of the whole body without requiring the patient to lie still for an excessive length of time.

The great bulk of work with the profile scanner has been devoted to experiments with samples to determine such characteristics as field of vision, uniformity, and cut-off points. Work is also in progress on a device to explore its response. At the end of the year, work was in progress on the construction of a three-dimensional isoresponse model for the scanner; it will serve as a standard for future investigations and for the proper operation of the machine on patients.

It is hoped that the profile scanner may be made quantitative, because more and more interest is being given to the quantity of radioactivity in a person's body. Present levels are exceedingly low, but the question of fallout has caused more persons to become interested in determining the exact amount; if present work on the profile scanner is successful, it may be possible to determine the total radioactivity in a person's body by passing him beneath it. In the course of this study, the radiation victims of the Y-12 accident were scanned by the device.



The Medical Division's human linear scanner.

Research associate Akiro Tsuya has devised a method of getting very roughly quantitative recordings of the field of vision of a scanning head or other detecting head. The method provides only an approximate answer, but it has the virtues of being automatic, provides a visible record, and can be done in a few minutes.

Another scanning problem under investigation is that of "background erase." The investigation includes not only the question of the best method of erasing background, but also whether such erasing is desirable. Such desirability will be investigated along with the quest for a practical erase circuit.

THYROID-UPTAKE PROGRAM

Special studies were begun during the year on the early uptake phase of radioactive iodine-131 in normal and hyperthyroid patients. Principal objective is the improvement of methods of obtaining early uptakes. By taking advantage of previous work done on the correction for neck background, and using a continuous recording device, staff members have been studying the effects of varying doses of drugs such as stable iodide and potassium perchlorate on thyroid physiology.

CLINICAL STUDIES

A most active program in the Medical Division is that concerned with total-body irradiation and bone-marrow transplantation. Further detailed studies have been made on biochemical changes and changes in morphology of bone marrow in patients with leukemia after a single massive dose of total-body irradiation. Bone-marrow transplantation has been attempted according to methods previously developed in the Medical Division.

Although some temporary favorable results have been obtained in children with acute leukemia, it is not felt that true transplantation has been clearly demonstrated. It is possible that some blast-cell leukemias respond to a single large dose of total-body irradiation with a suppression of the leukemic process and reactivation of normal blood formation. Efforts

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are now under way to determine the true place of the bone-marrow injections in this sequence of events.

In patients with subacute granulocytic and monocytic leukemia, in the adult age group, no favorable results have been attained, although transient depression of the leukemic process has ben demonstrated. During the past year, the division has improved its facilities for delivering total-body irradiation with cobalt-60. A special simple shielded source allowing a wide-angle beam distribution has been set up, and, in addition, the new Westinghouse two-headed cobalt-60 teletherapy machine has been used for this type of treatment.

During the year, considerable effort went into the development of methods for platelet separation and storage. Platelets are essential for treating the period of marrow aplasia following the massive irradiation. Biochemical studies have tried to characterize the results of the tissue breakdown, which is so striking immediately after these large doses of radiation. It is obvious that in leukemic patients, because of the large volume of highly sensitive cells, this tissue breakdown may be much more extensive and profound than might be expected with a similar dose to a normal individual.

Y-12 Radiation Accident

The radiation accident, which occurred at Y-12 on June 16, occupied the clinical staff of the Medical Division for the rest of the year, and is continuing to require major effort.

Extensive studies of blood and bone marrow and biochemical changes in the blood and urine were initiated as soon as the patients arrived at the hospital, and have been continued to the present.

During the early period of care of these patients, serious consideration was given to the use of bone-marrow transplantation. The facilities and techniques set up for the leukemia-radiation program were available, and a large number of potential bone-marrow donors were called into Oak Ridge. Relatives of the patients were selected, in the belief that they might offer genetically more suitable marrow. However, with the determination that the doses of radiation were somewhat lower than had been initially found, and after evaluation of the immediate clinical response, it was decided that marrow transplantation would not be used.

The patients showed a typical radiation response, and during the third and fourth week after radiation had pronounced thrombocytopenia. At this point a group of blood donors was kept on call so that fresh blood could be given promptly if necessary. However, the patients went into a recovery phase spontaneously, and no blood or platelet transfusions were required.

Extensive assistance was received from physicians outside the Medical Division in caring for the patients who were subjected to accidental radiation. Shields Warren, consultant to the U. S. Atomic Energy Commission, and Charles L. Dunham, director of the AEC Division of Biology and Medicine, visited the division shortly after the accident. Special arrangements for provision of tissues for transplantation were made with the help of Charles C. Congdon, Biology Division, Oak Ridge National Laboratory; and Joseph Ferrebee and Don Thomas of the Mary Imogene Bassett Hospital in Cooperstown, New York.

Continuing studies on biochemical aspects of the problem have been carried out with the cooperation of Louis H. Hempelmann, of the University of Rochester, and M. C. Goodall of Duke University. Special help on hematologic problems has been given by Eugene P. Cronkite of Brookhaven National Laboratory, and a research program involving the use of tritium-labeled thymidine has been carried out by Dr. Cronkite, Victor P. Bond, and Ted Fliedner, also of Brookhaven, with the help of Andrew Myron Johnson, medical student on a summer fellowship with the Medical Division, and permanent members of the division staff.

Studies on the clotting mechanism and related blood components have been done by Herbert Size, Jacques Gauthier, and John J. Bolger, all of Boston City Hospital. George T. Harrell, dean of the College of Medicine, University of Florida, has taken a special interest in the problem, and has arranged for some electrophoretic studies on the serum to be done by F. W. Putnam, professor of biochemistry at the University of Florida, to supplement the extensive studies done by Granvil C. Kyker's group at the Medical Division.

Among the Oak Ridge people who have participated to an extensive degree in the management of the radiation accident are C. R. Sullivan, Jr., Y-12 plant physician; Robert A. Charpie, assistant director, Oak Ridge National Laboratory; and H. J. McAlduff, Jr., deputy director, AEC Inspection Division. K. Z. Morgan, director of the ORNL Health Physics Division, and his staff, in a rushed effort to determine the dosage received by the men involved in the accident, carried on an experiment that required many staff members to go without sleep for about forty-eight hours. The information they obtained became available promptly enough to be used as a basis for deciding not to give bone-marrow transplantation to the irradiated individuals. L. K. Akers and H. K. Ezell, Jr., of the ORINS Special Training Division have carried out some special studies on the radioactive products in the urine.

All these efforts were in addition to the specific activities of the permanent, resident, technical, and nursing staffs of the Medical Division, almost all of whom have been involved in one way or another in caring for these patients.

(Editor's Note: Nominally, the information contained in this report does not extend beyond the period ending June 30, 1958. Because of the nature of the Y-12 incident, however, an exception is being made. The five patients under observation and treatment at the Medical Division were discharged from the hospital on July 30, and subsequently returned to work at the Y-12 plant. The men will be kept under observation for a considerable period of time, but the observation will be done on an outpatient basis.)

Massive Nitrogen Mustard Effects on Bone Marrow

A group of patients is being treated with large doses of nitrogen mustard with and without efforts at autologous marrow transplantation. An evaluation of hematologic effects of the dose is expected to provide information about the success or failure of the marrow transplantation.

Long-Range Clinical Programs

The Medical Division is continuing to study the treatment of various hematologic disorders with radioisotopes and chemotherapy. The total-body irradiation program has required the division's taking on a considerable number of patients with acute and subacute leukemia. A number of these are being followed in the hospital and on an outpatient basis. This has required an increased amount of hematologic work and has increased the outpatient load. In general, the total-body irradiation has been reserved for patients who have previously had an adequate trial of drug therapy. A continued long-range evaluation has been made of intravenous colloidal gold-198 in the treatment of chronic leukemia.

Patients with ovarian carcinoma have been studied with repeated surgical treatment and the use of intraperitoneal colloidal radioisotopes. A limited amount of work has been done with yttrium-90 and lutecium-177. Immediate chemical reactions on serous surfaces after intraperitoneal and intrapleural use of the rare-earth elements have continued to present a problem, but there is evidence of good therapeutic effect, at least from the yttrium-90. Intracavitary nitrogen mustard has also been studied in a limited number of cases in an effort to compare its effects with those of the colloidal radioisotopes.

Hyperthyroidism, carcinoma of the thyroid, and a few cases of heart and pulmonary disease have been treated with radioiodine. The most active research effort in these areas has been the study of thyroid remnants and small functioning metastases of carinoma, plus the special thyroid physiology studies in hyperthyroid patients, as previously mentioned.

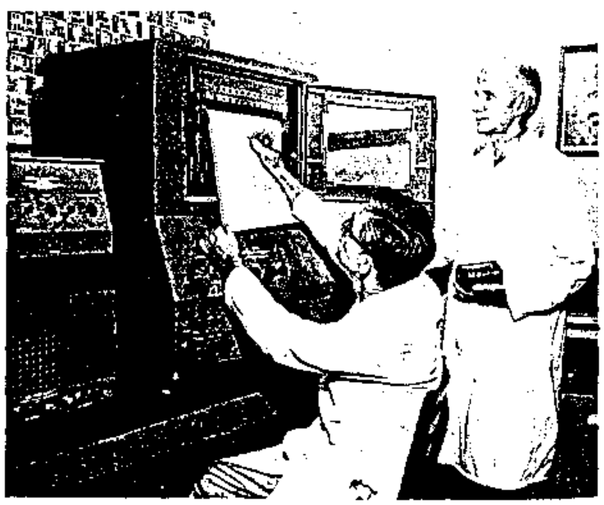
Clinical Teaching Program

The clinical staff of the Medical Division has continued to have a series of short-term residents who have participated in the clinical program. The treatment of patients with more or less routine forms of radioisotope therapy has been continued as a means of having clinical material for this teaching program.

In addition to the residency training program, members of the clinical staff have participated in special teaching activities in the Medical Division short courses and in the basic radioisotope techniques course given by the Special Training Division. They have also presented a number of lectures before various organizations outside of Oak Ridge.

Clinical Dosimetry Studies

The major effort on this program during the year involved continuation of the program initiated in Fiscal



Senior scientist R. L. Hayes (left) and David B. Camp, research participant from the University of the South, test the newly acquired automatic recording spectrophotometer.

Year 1957 on dogs and goats. Small-volume detectors were implanted in the walls of the intestinal tract of experimental animals. (The dogs represented single-stomach animals, the goats, multiple-stomach animals.) The test animals were given known doses of beta-emitting isotopes and, after recovery, it was possible, using certain calibration techniques, to determine the dose received by the intestinal mucosa of the animals at the site of implantation.

This dose to the mucosa was studied as a function of site of implantation, size of the animal, and motility of intestinal content (normal, constipated, and diarrheal). These studies served to emphasize extreme variations in dose caused by variation in gastrointestinal motility of the individual animals.

Study was expanded to an investigation of the concentration-time studies at different sites along the intestinal tract. This study enabled the investigators to make an indirect calculation of the average dose at the different sites investigated. The indirect determination was in excellent agreement with the dosimeter determination.

PRECLINICAL STUDIES

The experimental program of preclinical studies is summarized under three topics: rare-earth studies, protein metabolism, and topics of related interest. The studies in each topic during the past year have continuity with interests and objectives stated in previous reports.

Rare-Earths Program

Emphasis in the rare-earth studies has shifted from the tracer measurements of mobilization of various combinations of rare-earth elements and radioisotopes to the analysis and evaluation of these measurements and to the investigation of biochemical behavior of the elements.

The toxicity of several rare earths, particularly yttrium and lanthanum, was discovered to be greater than had been previously reported, with toxicity by the intravenous route considerably greater than by other methods. A complete tabulation of all toxicity measurements in various experimental animals by several routes of administration was compiled and included in a published report to permit additional interpretations for the series of elements. The report includes certain considerations of their chronic toxicity.

Protein Metabolism

The program in protein metabolism was represented by the experimental work for the doctoral degree performed by Arthur L. Kretchmar, Medical Division clinician, and administered in cooperation with the Department of Biochemistry, University of Michigan. The experimental work was completed and Dr. Kretchmar received his degree in February. In addition to the protein-metabolism work, related experimental studies were carried out during the period.

Calcium-47

Because of the radiation characteristics of calcium-47 that make it of potentially greater value in human studies than the calcium-45 now in general use, an attempt was made to produce a quantity of calcium-47 by neutron irradiation of enriched calcium-46 at Oak Ridge National Laboratory, but the attempt was relatively unsuccessful. These preliminary results do, however, indicate that it will be worth while to repeat the activation of the enriched material and to isolate the calcium-47 from other impurities before evaluation.

Animal Problems

During the year, the ORINS animal facilities were remodeled to some extent, and this remodeling will continue.

Difficulties have been encountered in maintaining a colony of specific-pathogen-free (SPF) rats. After a colony of rats had been destroyed because of an epidemic of respiratory disease, a new colony was transported by special carrier from New York and established in special cleaned, disinfected, and renovated quarters. After 60 days, respiratory symptoms were detected in the new colony; investigations indicated that the animals had been infected before their shipment to Oak Ridge. Plans are in progress to obtain a guaranteed SPF colony, to arrive in August of 1958.

Small-Animal Scanner

A linear scanner for small animals, to determine the longitudinal distribution of radioisotopes in the animal, was designed and constructed during the year. It is a simplified version of the man-sized scanner, and has been tested with surgical samples and human pathological material.

TELETHERAPY PROGRAM

Design, construction, and installation of a new 1300-curie, double-headed cobalt-60 teletherapy machine were completed during the year. The new unit

A double-headed radiation-teletherapy unit, using two 650-curie sources of radioactive cobalt-60, was installed in the Medical Division last spring.

is a compromise between the fixed-beam and continuously variable types of machines; each head has a revolving turret mounting six semipermanent collimators and one easily removable collimator, so that seven different beam sizes and intensities are readily available in each head at any time.

The two heads, which revolve about the patient, permit the diseased tissue to receive a large amount of radiation while the surrounding tissue and skin receive a comparatively small amount.

Little actual therapy was carried out with the new machine or the division's other teletherapy units; standard testing to determine isodose curves and optimum operating procedures was undertaken, but no real activation of the teletherapy program is planned until the arrival of Francisco Comas, a former resident physician at the Medical Division, to assume direction of the program in July 1958.

GENERAL

In the course of the year, Cyril L. Comar and Robert Wasserman finished their work at the Medical Division and are now at Cornell University. Newcomers to the division included A. C. Morris, Jr., instrument engineer; Beecher W. Sitterson, chief clinician; and Fred Snyder, assistant scientist.

Marshall Brucer, chairman of the Medical Division, and Granvil C. Kyker, chief of preclinical research, assumed the offices of president and program chairman, respectively, of the Society of Nuclear Medicine. Drs. Brucer and Gould A. Andrews, chief of clinical services, were prevented from attending the annual meeting of the SNM, over which Dr. Brucer was to preside, by the necessity of taking care of the Y-12 accident victims, but Medical Division members D. A. Ross, chief of medical physics, R. L. Hayes, senior scientist, and Dr. Kyker all attended the meeting and took active part in presenting papers and a course in thyroid-uptake calibration. Mrs. E. H. Anderson, research associate, was in charge of a special display of "midget" exhibits, prepared by the Medical Division, at the same meeting.

A patent on "mock-iodine," the barium-cesium mixture used in the thyroid-uptake calibration program, was issued to Dr. Brucer.

APPENDIX III
Medical Division

CONSULTANTS TO THE MEDICAL DIVISION

ALABAMA
- Medical College of Alabama
  - William H. Riser

ARKANSAS
- University of Arkansas Medical Center
  - Howard J. Barnhard

CALIFORNIA
- City of Hope Medical Center
  - Melville L. Jacobs
- Eden Hospital
  - Ralph M. Kniseley
- University of California at Los Angeles
  - Benedict Cassen
- UCLA Medical Center
  - Raymond L. Libby
- University of Southern California School of Medicine
  - Franz K. Bauer
  - Henry L. Jaffee

COLORADO
- University of Colorado
  - Jerry K. Aikawa

DISTRICT OF COLUMBIA
- AEC, Washington, D. C.
  - Paul C. Aebersold

FLORIDA
- Florida State Board of Health
  - Lorenzo L. Parks
- Halifax District Hospital
  - Herbert D. Kerman
- Private Physicians
  - Louis M. Orr
  - Samuel W. Root
- University of Florida
  - George T. Harrell
  - Francis E. Ray

GEORGIA
- Emory University School of Medicine
  - Bryan Redd
  - H. Stephen Weens
- Medical College of Georgia
  - Claude-Starr Wright

ILLINOIS
- Cook County Hospital
  - Irvin F. Hummon

KANSAS
- University of Kansas
  - Frank E. Hoecker
- University of Kansas School of Medicine
  - Galen M. Tice

KENTUCKY
- University of Louisville School of Medicine
  - Harold F. Berg
  - William M. Christopherson
  - Ji-loong Ling

LOUISIANA
- Ochsner Clinic
  - William R. Arrowsmith
  - Paul J. Murison
- Tulane University
  - John U. Hidalgo
  - Robert T. Nieset

MARYLAND
- Martin Company
  - Stanley H. Clark
- National Institutes of Health
  - George Z. Williams

MASSACHUSETTS
- Harvard University Medical School
  - A. Stone Freedberg

MICHIGAN
- University of Michigan School of Medicine
  - Jere Bauer
  - Halvor N. Christensen
  - Adam A. Christman
  - M. J. Coon
- Wayne University College of Medicine
  - James E. Lofstrom

MISSISSIPPI
- University of Mississippi Medical Center
  - Robert D. Sloan

MISSOURI
- Private Physician
  - Wendell G. Scott
- University of Missouri School of Medicine
  - Walter J. Brudette

NEBRASKA
- Creighton University School of Medicine
  - James F. Kelly, Jr.
- University of Nebraska
  - Howard B. Hunt
  - Merle M. Musselman
  - Arthur Tuma

NEW YORK
- Francis Delafield Hospital
  - Carl B. Braestrup
- Hospital For Joint Diseases
  - Milton Friedman
- New York University—Bellevue Center
  - Sidney Rubenfeld
- Private Physician
  - Norman Simon
- State University of New York
  - Warren Glaser
- Syracuse Memorial Hospital
  - Alfred S. Berne
  - G. Ferlazzo
  - Paul A. Riemenschneider

NORTH CAROLINA
- Bowman Gray School of Medicine
  - Camillo Artom
  - Isadore Meschan
- Duke University School of Medicine
  - William G. Anlyan
  - Harold W. Lewis
  - Robert J. Reeves
  - C. R. Stevens
  - Malcolm P. Tyor

University of North Carolina
John H. Ferguson
Charles D. Van Cleave

NORTH DAKOTA
University of North Dakota School of Medicine
William E. Cornatzer

PENNSYLVANIA
Temple University School of Medicine
R. C. Baldridge

SOUTH CAROLINA
Medical College of the State of South Carolina
John C. Hawk

TENNESSEE
Carson Newman College
Carl T. Bahner
Oak Ridge Hospital
Robert P. Ball
Robert R. Bigelow
Dana W. Nance
W. W. Pugh, Jr.
C. J. Speas
Paul E. Spray
University of Tennessee College of Medicine
David S. Carroll
Alfred P. Kraus
Carl E. Nurnberger
John L. Wood
Vanderbilt University
Herbert Francis
Granville Hudson
C. C. McClure
Veterans Administration Hospital
George R. Meneely

TEXAS
M. D. Anderson Hospital
Gilbert H. Fletcher
Robert J. Shalek
Baylor University
Vincent Collins
Harold Tivey
Brooke Army Medical Center
J. A. Isherwood
University of Texas Medical Branch
Ludwik Anigstein
Robert N. Cooley
Wendell D. Gingrich
William C. Levin
Wiktor W. Nowinski
Martin Schneider
Howard G. Swann

VIRGINIA
Medical College of Virginia
Frederick B. Manderville
University of Virginia
George Cooper
Kenneth R. Crispell
George R. Minor

WASHINGTON, D. C.
U S Veterans Administration
Lyndon E. Lee

WISCONSIN
University of Wisconsin
Edgar S. Gordon

PUERTO RICO
University of Puerto Rico
Conrado Asenjo

TELETHERAPY EVALUATION PROGRAM

INSTITUTION	REPRESENTATIVE ON TEP
Baylor University	Vincent Collins
Creighton University	James F. Kelly, Jr.
Duke University	Robert J. Reeves
Emory University	H. Stephen Weens
Louisiana State University	
Medical College of Virginia	Frederick B. Mandeville
New York University (Bellevue Medical Center)	Sidney Rubenfeld
State University of New York (Syracuse)	Paul Riemenschneider
University of Alabama	William H. Riser, Jr.
University of Arkansas	Howard J. Barnhard
University of Kansas	Galen M. Tice
University of Louisville	Ji-toong Ling
University of Mississippi	Robert D. Sloan
University of Nebraska	Howard B. Hunt
University of Southern California	Henry L. Jaffe
University of Tennessee	David S. Carroll
University of Texas (Medical Branch)	Robert N. Cooley
University of Texas (M. D. Anderson Hospital)	Gilbert H. Fletcher
University of Virginia	George Cooper
Vanderbilt University	Herbert C. Francis
Wake Forest College	I. Meschan
Wayne University	James E. Lofstrom

MEDICAL DIVISION SEMINAR SERIES

THYROID-UPTAKE SEMINAR FOR TECHNICIANS
August 19-23, 1957

Olive Bell .... Kentucky Baptist Hospital, Louisville, Kentucky
Phyllis Canup .... University of North Carolina School of Medicine, Chapel Hill, North Carolina
Mrs. Barbara M. Covey .... VA Hospital, Atlanta, Georgia
Mrs. Thelma Eubanks .... East Tennessee Baptist Hospital, Knoxville, Tennessee
Robert Gray .... Holston Valley Community Hospital, Kingsport, Tennessee
Margaret Keefe .... Queens General Hospital, Jamaica, New York
Robert D. Lee .... East Tennessee Baptist Hospital, Knoxville, Tennessee
T/Sgt. George W. Lucas .... Department of Radiology, 388 2nd School Group, Gunter Air Force Base, Alabama
Mary Ann Matassa .... St. Agnes Hospital, Baltimore, Maryland
Walter Mayes .... Providence Hospital, Mobile, Alabama
Mrs. Jean King Moore .... Holston Valley Community Hospital, Kingsport, Tennessee
Maryanne Nelson .... VA Hospital, Iowa City, Iowa
Mary H. Rennie .... VA Hospital, Ann Arbor, Michigan
Dorothy M. Roth .... VA Hospital, Louisville, Kentucky
Edith Sharp .... University of Indiana, Indianapolis, Indiana
Mrs. Kathryn Sharpe .... Duke University, Durham, North Carolina
Mike D. Stephens .... Watts Hospital, Durham, North Carolina
Jack W. Wright .... Coatesville Hospital, Coatesville, Pennsylvania

SEMINAR FOR PATHOLOGISTS: DIAGNOSTIC USES OF RADIOISOTOPES
November 11-16, 1957
February 10-15, 1958

F. Wells Brason .... Harrisburg Hospital, Harrisburg, Pennsylvania
Victor B. Buhler .... St. Joseph's Hospital, Kansas City, Missouri
Gerald S. Dean .... Highland Park Hospital, Highland Park, Illinois
Frank J. Eurs .... Woman's Hospital, Detroit, Michigan
Herbert L. Goodman .... Bryn Mawr Hospital, Bryn Mawr, Pennsylvania
Louis P. Hastings .... St. Francis Hospital, Hartford, Connecticut

Francis S. Jones ✓ ... University of Tennessee Memorial Research Center and Hospital, Knoxville, Tennessee
Elizabeth Khayat ... The Jamaica Hospital, Jamaica, New York
Joseph R. Kraft ... St. Francis Hospital, Peoria, Illinois
Morton H. Kulesh ... University of Nebraska College of Medicine, Omaha, Nebraska
Christie E. McLeod ... 28 Crescent Street, Middletown, Connecticut
Harlan L. Papenfuss ... 2315 S. 17th Street, Lincoln, Nebraska
William G. Rice ... Mount Carmel Hospital, Columbus, Ohio
Henry A. Rothrock ... Chester County Hospital, West Chester, Pennsylvania
Olin Wiland ... Reid Memorial Hospital, Richmond, Indiana

ISOTOPES USED BY MEDICAL DIVISION

Isotope	mc
Calcium-45	1
Chromium-51	11
Rachromate	8
Cerium-Praseodymium-144	20
Cesium-Barium-137	5
Cobalt-60	1,294,000.6175
Cobalt Alloy	2,665
Europium Powder	736
Gold-198	2,680
Iodine-131	4.75
Oriodide	3,640
Radiocaps	17.91
Risa	19
Rose Bengal	16
Iodine-132	10
Iron-59	3.25
Phosphorus-32	289
Scandium-46	3
Sulfur-35	63
Yttrium-90	595
Yttrium-91	75
Iron-59 (P)	3
Rubidium-86	20
Potassium-42	20
Triolein	2
Sodium-24	23
Barium-133	8
Thulium	1
Niobium-95	2
Promethium-147	20
Calcium-47	Less than 0.01

ORINS HOSPITAL PATIENT DAYS

July	584
August	539
September	502
October	490
November	502
December	366
January	412
February	458
March	592
April	538
May	467
June	514
Total Patient Days	5964
Average Per Month	497
Average Per Day	16.3

RESIDENT PHYSICIANS

Edmund B. Andrews ... University of Michigan Hospital, Ann Arbor, Michigan
Bernd Bach ... East Tennessee Baptist Hospital, Knoxville, Tennessee
William R. Blade ... East Tennessee Baptist Hospital, Knoxville, Tennessee
Hans H. Faust ... East Tennessee Baptist Hospital, Knoxville, Tennessee
William D. Huffines ... University of North Carolina School of Medicine, Chapel Hill, North Carolina
Alberto Manaresi ... Mount Sinai Hospital, Minneapolis, Minnesota
K. J. Momose ... Massachusetts General Hospital, Boston, Massachusetts
Misha D. Newman ... Charity Hospital, New Orleans, Louisiana
John T. Pollard ... Massachusetts General Hospital, Boston, Massachusetts
Mario Perez-Reyes ... Prince George's General Hospital, Cheverly, Maryland
Alvin Segel ... Cleveland City Hospital, Cleveland, Ohio
Jean G. Tessier ... Royal Victoria Hospital, Montreal, Quebec, Canada
Alfred L. Weber ... Massachusetts General Hospital, Boston, Massachusetts

POSTRESIDENT ASSISTANTS

Orren W. Hyman, Jr. ... St. Mary's Hospital, Knoxville, Tennessee
C. G. Papavasiliou ... Boston City Hospital, Boston, Massachusetts

RESIDENT IN EXPERIMENTAL MEDICINE

Robert Nightingale ... Iowa Methodist Hospital, Des Moines, Iowa

NONEMPLOYEE VISITORS

Nazeer Ud-Din Ahmad ... West Pakistan Health Service, West Pakistan, Pakistan
Lan-Chang Chiang ... National Kwei Yang Medical School, Kwei Yang, China
Junichi Fujita ... The Second National Hospital of Tokyo, Tokyo, Japan
Andrew Myron Johnson ... Vanderbilt University, Nashville, Tennessee
Luis Amoros-Marin ... University of Puerto Rico, San Juan, Puerto Rico
Walter Elmore Nance ... Harvard Medical School, Cambridge, Massachusetts
Efraim Otero-Ruiz ... Javeriana University School of Medicine, Bogota, Columbia
John H. Rust ... University of Chicago, Chicago, Illinois
V. M. Sivaramakrishnan ... University Biochemical Laboratory, A. C. College, Madras, India
William B. Stavinoha ... University of Texas Medical Branch, Austin, Texas

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Oak Ridge Institute of Nuclear Studies

Thirteenth Annual Report

OPERATING UNDER CONTRACT

WITH THE

United States Atomic Energy Commission

JUNE 30, 1959

Medical Division

THE research program of the Medical Division during the past year has involved three major emphases: total-body irradiation, scanning, and rare-earth studies. The clinical use of total-body irradiation has been an active research interest of the division, in one form or another, for several years. During the past two years, this activity has become a major area of interest through the specific problem of the treatment of patients with leukemia or other widespread forms of cancer with large doses of radiation from multiple external beams. Further emphasis was given to this problem this year through the clinical studies of several patients accidentally exposed to total-body irradiation in the accident that occurred at the Y-12 plant in Oak Ridge on June 16, 1958. (See ORINS Twelfth Annual Report.)

An associated problem involves studies of the replacement of bone marrow following irradiation to get the patient over the period of primary radiation damage. In support of this clinical program, an extensive program of amino-acid analysis has been instituted and developed.

The second major research emphasis of the division during the year has been in the field of investigating various techniques of external scanning for diagnosis and clinical assessment of patients. This program is based on a close working relationship that has existed for several years between medical specialists in ORINS and electronic and instrument specialists at Oak Ridge National Laboratory. It therefore represents one of the activities of the division that is peculiarly appropriate for a research hospital located at an Atomic Energy Commission installation.

The third area of major interest has been that of continuing studies at the preclinical level of the rare-earth isotopes. There are important clinical potentialities of several of these isotopes, but animal studies have shown unsuspected toxicity that must be followed up before further human work can be attempted. These studies have a broader application than that of the Medical Division's specific interest because of widespread concern over fission products. The general understanding of their biological behavior, metabolism, and toxicity is therefore of wide value.

Closely integrated with the research program, is a continuing program of clinical training that has been maintained at an increased level during the year. In this period, much of the training activity of the division has been concentrated into developing formal courses, thereby hoping to economize on staff time that might be diverted from research to training activities. The Medical Division has devoted approximately one week out of every month to the presentation of a series of courses in some aspect of the clinical use of radioisotopes.

In addition to the major program emphases of the division, a number of smaller research efforts grow out of individual staff interests and more especially out of projects undertaken by visiting scientists and other temporary personnel. For example, a visiting Japanese scholar has adapted the scanning technique to a method of assessing the clinical value of various detectors. One of his colleagues has been primarily interested in the energy of scattered radiation from external beams of radiation. In another instance the rather sudden unexpected availability of a new short-lived isotope caused the entire staff to concentrate on animal, clinical, and instrumental problems with calcium-47. Many of these problems are dependent upon individual research interests but nevertheless do support the over-all divisional programs. It should be noted that all three of the major projects were many years ago problems of incidental interest. Therefore, these temporary excursions for the preliminary exploration of new ideas are encouraged whenever possible.

The year has seen a reorganization of the Medical Division, with changes of title for some staff members. Marshall Brucer continues as chairman of the division, and G. A. Andrews, formerly chief of clinical services, has been named as associate chairman. B. W. Sitterson succeeds Dr. Andrews as chief of clinical services, and Granvil C. Kyker becomes chief of preclinical research.

Ralph M. Kniseley, former pathologist for the division, has returned after four years in California, to become chief of clinical training and research. D. A. Ross continues as chief of medical physics.

Progress has also been made during the year in improving the physical facilities of the Medical Division, has returned after four years in California, to steps are being taken to add the D Wing of the old Oak Ridge Hospital to the present Medical Division E Wing. This two-and-one-half story structure will add 25,650 square feet of hospital and laboratory space to the division's existing facilities. It is expected that the clinical section of the Medical Division will move into the new wing within the next year.

Another addition will become the primary facility for the total-body irradiation program. The extra space will also enhance the study of total-body dosimetry and make possible the extension of metabolic studies to humans.

The training program will also benefit from the addition of the D Wing. The Medical Division's whole training activity has been directed to physicians who already have specialty boards in other fields of practice. The present training facility, still incomplete, will be finished when the clinical section moves into the new wing.

TOTAL-BODY IRRADIATION

The study of total-body irradiation and the treatment of radiation injury has continued to be the most active clinical program in the Medical Division. Changes after total-body irradiation of leukemic patients are quite different from those caused by the same dose of radiation in a normal patient. In a leukemic patient, the period of bone-marrow aplasia comes on much more rapidly, and the symptoms of hemorrhage and infection are likely to occur within the first three or four weeks after irradiation, instead of between the fourth and sixth weeks as in patients who are normal at the time of exposure.

Leukemic cells in general seem to be more rapidly destroyed by radiation than are normal blood and marrow cells. In spite of this fact, efforts to treat leukemia with marrow transplantation have been discouraging. Only patients in unfavorable stages of leukemia have been considered legitimate for treatment, and such patients generally do not survive long after a large dose of total-body irradiation. Clear-cut evidence of the survival of the administered marrow has not been obtained; on the other hand, it has been demonstrated that it is possible to produce a distinct remission by radiation alone, under certain circumstances, in acute leukemia.

Medical Division staff members have carefully studied the experience and treatment of the group of Yugoslavian patients that were involved in a total-body irradiation accident in October 1958. These studies were compared with those made of the patients treated at the Medical Division after the Y-12 irradiation incident in June 1958. The apparent success of marrow administration in the Yugoslavian patients offers some encouragement for the pursual of this technique as a means of treating radiation injury. However, the fact that permanent survival of the marrow grafts was not achieved with the Yugoslavian patients offers little encouragement to the effort to abolish leukemic cells completely and permanently by means of radiation.

Studies have been started on a few patients who do not have leukemia or any primary blood disease, but who have widespread metastatic neoplasms. These patients are subjected to total-body irradiation in doses comparable to those used for leukemia. Because these patients have more or less normal blood formation, it is possible to obtain valuable information about the effects of irradiation on blood and bone marrow.

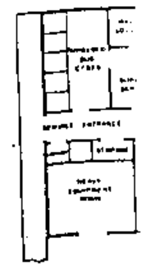
Total-Body Irradiation Dosimetry

Dose-depth relationships in the total-body irradiation situation are being investigated, using water phantoms designed to simulate a patient's body. Similar studies on total-body phantoms are planned as soon as the new total-body irradiation facility has been built and equipped.

Amino-Acid Studies

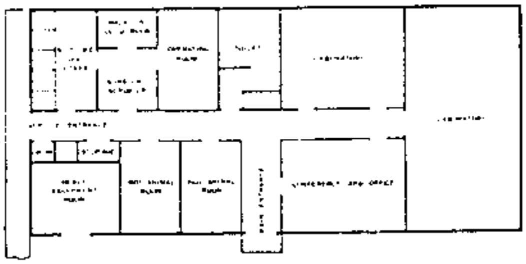
Closely connected with the clinical program of total-body radiation, is the biochemical analysis of amino acids. Amino acids excreted by humans after total-body irradiation are of interest from several points of view. Medical Division studies are directed at the levels of excretion of taurine and beta-aminoisobutyric acid as a possible biochemical index of the level of irradiation. It appears, from results at present available, that both taurine and beta-aminoisobutyric acid are excreted in greater quantity after total-body irradiation, but that only beta-aminoisobutyric acid levels can be correlated with dosage of irradiation over the 60-to-300-rad (radiation absorbed dose) range.

A second promising line of interest that may yield information on the effect of irradiation on intermediary amno-acid metabolism is the observation that humans accidentally irradiated do not excrete free serine, whereas this amino acid is present in normal persons and in persons who have recovered from the effects of radiation exposure. This result is probably related

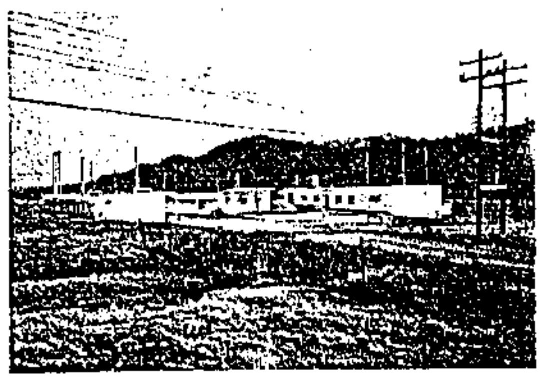


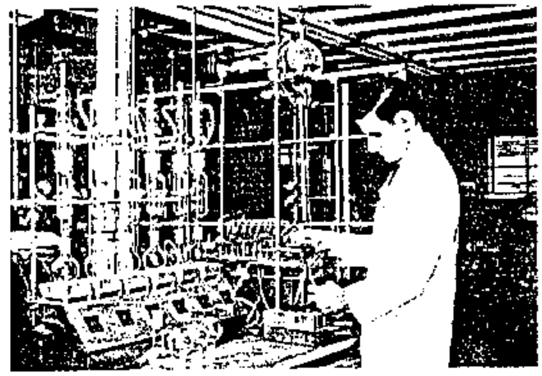
The newl
extensive

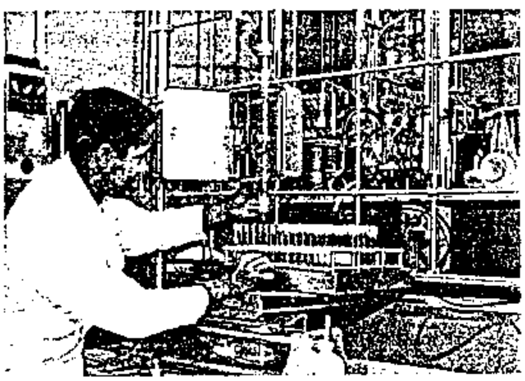
ANIMAL LABORATORIES

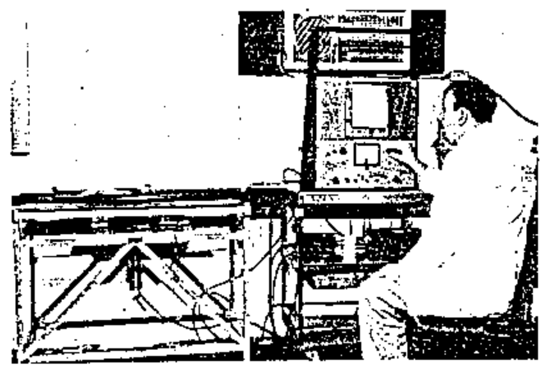


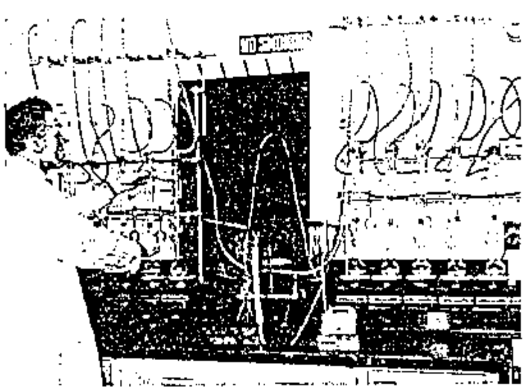
HIGH-LEVEL BUILDING











The newly constructed addition to the animal laboratories, pictured in the scenes above, facilitate the extensive preclinical studies that the Medical Division conducts with small animals.

to the dynamics of exchange between glycine and serine. This exchange is known to occur readily, and, therefore, the presence of normal levels of glycine is of particular interest. A possibility is that irradiation in some way blocks the glycine-serine exchange.

Y-12 Plant Radiation Accident Patients

After their discharge from the hospital on July 30, 1958 (as reported in the ORINS Twelfth Annual Report), the patients from the Y-12 plant radiation accident of June 16, 1958, have been followed at periodic intervals as outpatients to ensure proper medical care should any condition requiring such care become apparent, and to obtain information concerning the clinical effects of total-body irradiation in normal persons.

Three patients who received relatively low doses of radiation returned to work six weeks after the accident, and the remaining ones returned to work after twelve weeks. Aside from minor clinical symptoms, which subsequently improved, follow-up clinical, hematological, and biochemical studies have shown a maintenance of the normal status to which the patients returned.

CONTINUING CLINICAL PROGRAM

The division has continued its efforts to study hematologic disorders by means of radioisotopes, with special interest in patients who might be suitable for splenectomy and in efforts to evaluate these patients by means of radioactive chromium studies. Also of interest is comparison of assays of splenic tissue obtained at operation with the preoperative external-counting results. Among the patients sudied is a group with long-standing polycythemia vera who have developed various complications involving marrow fibrosis and blood changes suggesting leukemia. Some of these patients are also helped by splenectomy. Efforts are being made to clarify some of the clinical and laboratory features of these syndromes.

The long-range study on carcinoma of the ovary has continued to yield results indicating that repeated surgical attack upon the more chronic types of ovarian carcinoma is justified. Several long-range patients have continued in complete remission after multiple laparotomies. The use of radioactive gold intraperitoneally is being continued in selected cases to supplement excision of the larger masses. Internal radiation is also used in certain selected situations.

A number of patients with carcinoma of the thyroid have been studied in addition to the special group having small remnants of functioning tissue in the neck. The use of large test doses of radioiodine has yielded evidence of small metastases in some patients who appear to be entirely negative on the basis of tracer doses previously used. The larger doses do not have any more favorable percentage distribution, but because the counting rates become much elevated over background, it is possible to discover very small or slightly functioning lesions with large test doses in the 2- to 10-millicurie range.

Both the stationary and moving-source teletherapy units in the division are being used in continuing clinical studies on selected patients by a full-time staff member qualified in radiotherapy.

The treatment of hyperthyroidism and various types of goiter without carcinoma has continued chiefly as a teaching procedure. Certain types of research information have been obtained on these patients whose treatment is otherwise more or less routine.

RARE EARTH STUDES

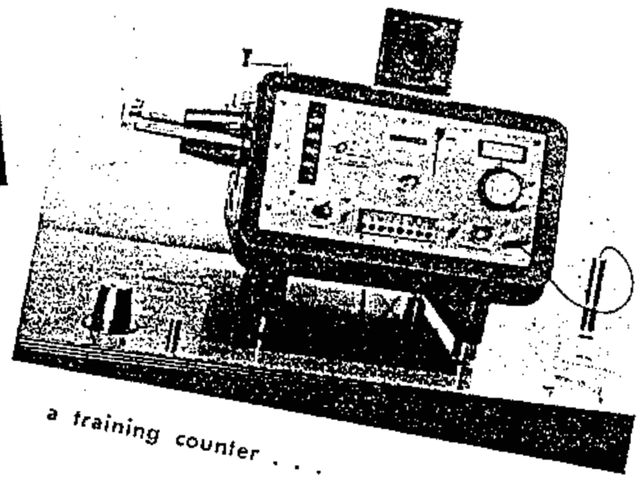
Interest in potential therapeutic applications of isotopes of rare earths continues, but more emphasis is being placed on their diagnostic and instrumental uses. Current experimental work has included (1) an extensive quantitative study of excretory patterns of rare earths by tracer analysis in surgically prepared dogs, (2) evaluation in rats of a commercially prepared "colloid" complex of yttrium with protein and phosphate, (3) evaluation of a small-animal linear scanner for rapid screening of internal behavior of radioisotopes, (4) the introduction of methodology and preliminary use of the intralymphatic route of administration for studying selective irradiation of lymph nodes by beta emitters, (5) radioisotopic distribution after previous exposure to large body burdens of stable element, and (6) an introductory approach to the effect of rare earths on selected enzyme systems. Although related medical interest in these elements has decreased somewhat, new causes have developed to study their poorly understood biochemical behavior, stemming from their recent and rapid industrial development. Consequently, study of these and related problems continues.

Additional approaches include (1) interaction and compound formation with selected biochemicals, (2) the internal biochemical stability of various compounds by a comparison of their mobility with the linear

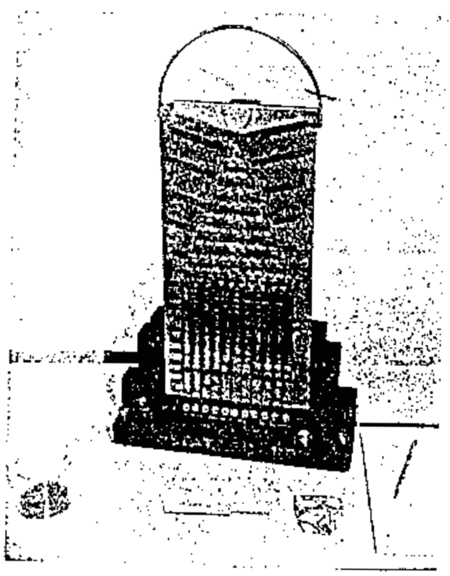
MEDICAL DIVISION TRAINING AIDS

include . . .

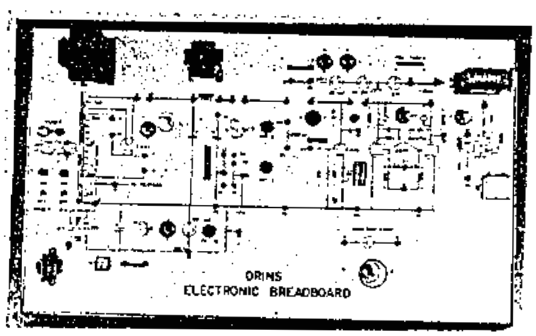
A goldfish experiment . . .



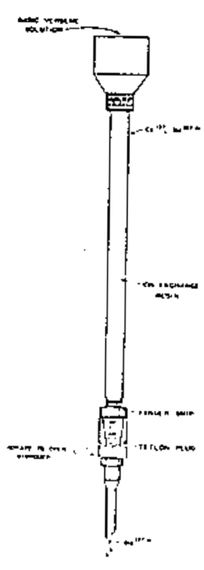
a training counter . . .



a statistics board . . .



an electronic breadboard . . .



and a half-life
demonstrator.

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scanner, and (3) their transport and excretion as indicated by hemodialysis.

Lipid Metabolism

Present studies on lipid metabolism are a direct outgrowth of the rare-earth work. Earlier work on various phases of distribution and toxicity studies disclosed an acute hepatic lesion in rats—an unexpected observation, since various workers had reported these elements to be relatively innocuous by other routes. The lesion, observed to be one of acute fatty infiltration, was recognized to be a unique way to study both the biochemical nature of the rare-earth elements and fundamental questions of lipid metabolism. The latter is now the major experimental problem.

The first study phase was one of characterizing this fatty infiltration by observing the influencing factors. These include (1) the species of mammal (especially noticeable in rats), (2) the strain of inbred rat and the sex, (3) the effect of fasting, (4) the effect of both depletion and of supplementation of various endocrine secretions, (5) the effect of lipotropic agents, (6) the effect on specific body depots of fat, and (7) the general question of mechanism—that is, mobilization of body fat *versus* synthesis of new liver fat. Superimposed on these factors is an evaluation of the individual members of the lanthanide series of elements that cause this biochemical lesion.

This problem of lipid metabolism in a specific setting of the rare-earth biochemistry is expected to be a major and lengthy one. It centers in a major area of biochemistry and provides the first experimental evidence that the lanthanons can involve specific metabolic interrelationships. Current studies emphasize the analytical fractions of the various types of lipids, cellular fractions, turnover studies by radioactive tracer analysis, and oxidative enzyme systems. The work has required several additions to the instrumentation, calling for considerable attention to the study and procurement of critical apparatus and to new methodology.

Animal Laboratories

Changes made in the animal-laboratory facilities represent a new environment for effective work. These include addition of a new building and improvements of existing space. The new building provides some 3100 square feet of floor area, divided among a large metabolic laboratory, a smaller laboratory with a radiochemical hood, a conference room, two small-animal rooms, a suite of three rooms for large-animal work, and accessory rooms for equipment, lockers, and sanitary facilities.

Other improvements include some remodeling of a small separate building to provide isolated housing for a breeding colony of specific-pathogen-free animals, modifications of the large-animal shed, installation of a small teletherapy unit, a breezeway connecting the two main buildings, and general area improvements.

Distribution of "Nonabsorbable" Radioisotopes in Humans

A program of tracer studies on humans of orally ingested radioisotopes considered to be normally nonabsorbable by the intestinal tract has been initiated. Lanthanum-140 is being used at present. Initial purpose of this program is to estimate the dose received by the lower intestinal tract as a result of the ingestion of such material. Previous experience in animal studies involving surgical implantation of small volume dosimeters along the intestinal tract forms the basis for this method of dose estimation.

The study is an attempt to measure the extremes of variation among individuals, rather than to obtain average dose data. Animal studies have shown remarkable variations in dose depending on the experimentally controlled state of intestinal motility. In addition to the estimation of dose to the intestinal tract, these studies also provide information on the actual intestinal-tract absorption and body retention when urinary assay and whole-body counting techniques are used. Maximum permissible concentrations of these types of radioisotopes are at present based primarily on animal distribution data.

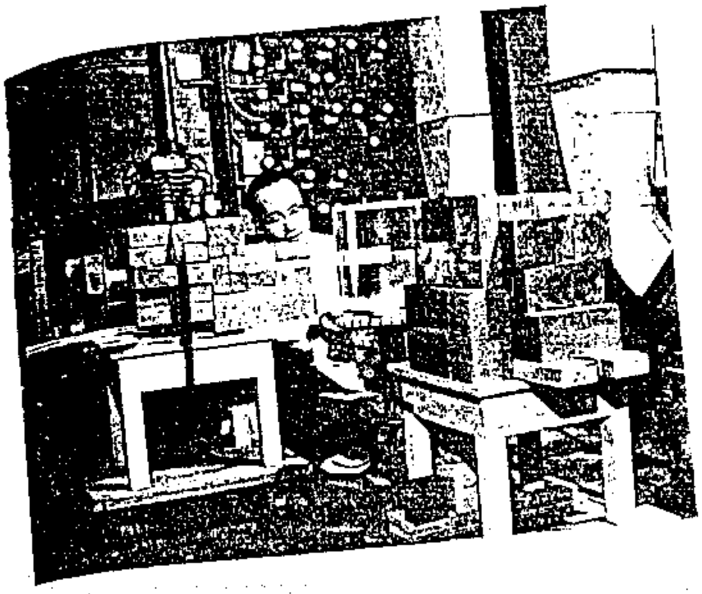
DIVISION TRAINING PROGRAMS

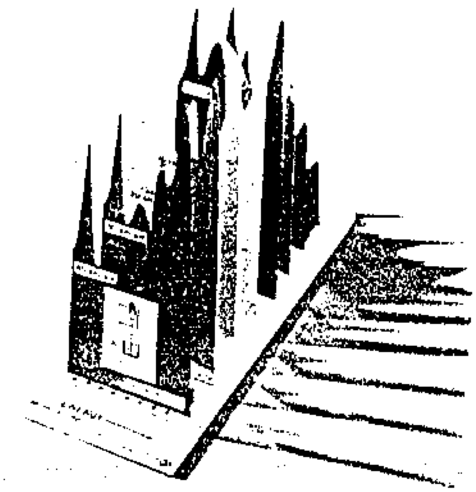
Clinical Training Program

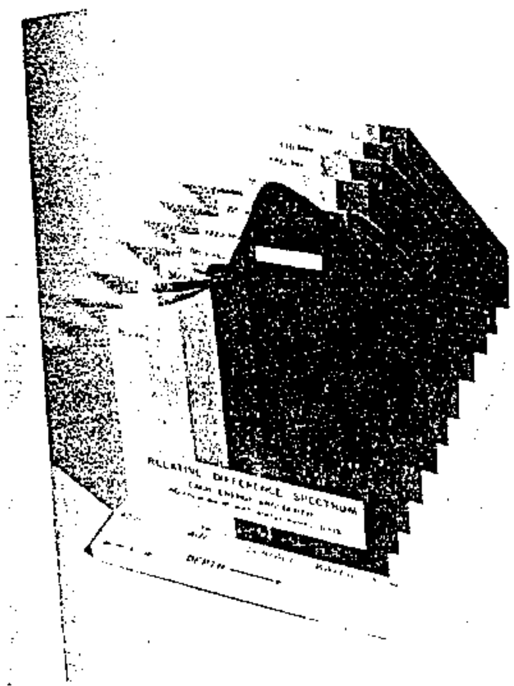
The training program for physicians at the Medical Division has expanded to the point where applications exceed accommodations. Two main programs are in effect: short- and long-term residencies and instructional seminars up to a week in duration.

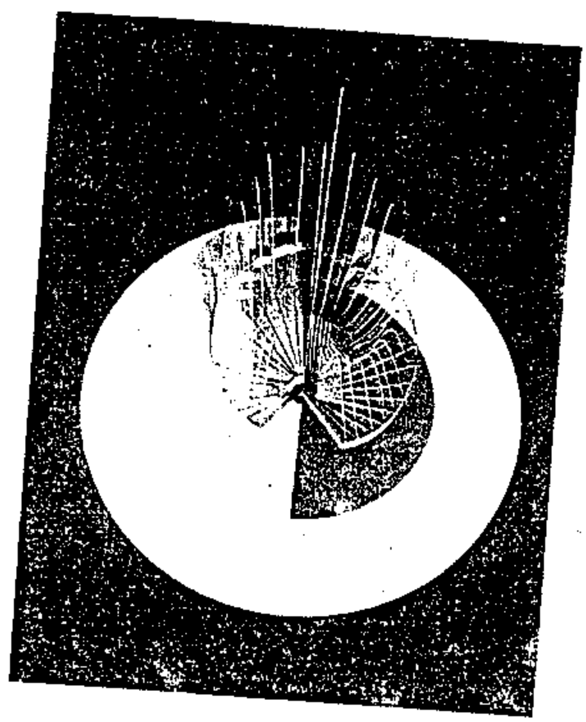
Short-term residencies, three or four months in length, are offered in such fields as medicine, surgery, radiology, and pathology. Usually, a physician comes to the division in the latter part of his residency, and credit toward specialty board qualifications is granted through the parent institution. Longer training is available through the one-year residency in experimental

RADIOISOTOPE SPECTRA









Yoichiro Umegaki, professor of radiology at Shinshu University in Japan, has spent a year at the Medical Division, working on various kinds of spectra in diagnostic and therapeutic applications of radioisotopes. Dr. Umegaki is shown at the upper left, with his apparatus for measuring angular scatter in water. His gamma-ray spectra of mock-iodine are at upper right. Below, left to right, are the difference spectra of cobalt-60, and angular scattering spectra of cesium-137.

medicine and the postresident assistantship in radiology.

During the training period, a variety of learning experiences is made available. Included are formal ward rounds, with reviews and discussions of all patients and examinations of roentgenograms and histologic sections, in which staff physicians, including internists, radiologists, and pathologists participate. Discussions include rationales of therapy and the possible usefulness of various radioisotopic therapeutic and diagnostic measures. The group also attends the regular Thursday-night scientific conferences on the division's programs, frequently attended by visitors who present subjects of their special interests. Participants are usually enrolled in the four-week basic radioisotope techniques course offered by the ORINS Special Training Division and, where feasible, attend the shorter instructional courses of the Medical Division.

In addition to routine patient care, supervised instruction is given in the use of isotopes for diagnosis and therapy and in the use of various kinds of electronic equipment, with frequent informal sessions concerning procedures or special apparatus. Related reading material in various forms is available in the Medical Division reading room and at the ORINS Technical Library.

Residents in attendance for long periods are expected to participate in a research project—in some cases, part of a project already under way, in others, a project initiated by a participant in cooperation with clinical and preclinical staff members.

The program of instructional seminars was begun during the year to meet increased demand for such training, with an average of one course a month on various topics. Preclinical I and II courses (one week each) include lectures, demonstrations, and laboratory exercises in basic medical uses of isotopes. An advanced third week has been designed in cooperation with the American Society of Clinical Pathologists to meet Atomic Energy Commission clinical requirements for diagnostic uses, with Preclinical I and II material recommended as prerequisites. These courses will be repeated in the coming year, and others are planned.

Medical Division residents and employees have priority of admission for these courses. Twenty participants are accepted for courses that include laboratory sessions, and forty in lecture-demonstration seminars. The faculty is composed primarily of ORINS personnel, with outside speakers for special topics.

During the fiscal year 1958-59, training was provided for thirteen resident physicians, two postresident physicians, one resident in experimental medicine, four nonemployee visitors, and two visiting scientists; in addition, there was a total of 118 student-weeks' attendance at the formal seminars and instructional training courses.

The preclinical staff participated in six of the one-week courses; about half of the teaching involving preclinical work was carried out at the animal laboratories, and the other half in the training room adjoining the hospital laboratories.

Electronic Training Aids

Because a basic introduction to electronic instrumentation is of great value in radioisotope training, students of courses given at the Medical Division are being provided with such instruction. To implement this introduction in the classroom, six "electronic breadboards" have been built. Students learn to construct circuits that demonstrate such electronic functions as rectification, transformation, amplification, regulation, detection, potentiometer action, and the Eccles-Jordan flip-flop circuit, culminating in a complete, working Geiger-Mueller counter. The warm reception by the two classes who have received this training indicates that it meets a defnite need.

Five modified Mediac counters are being used to instruct students in laboratory counting techniques. The modification permits the detection of radiation with an external Geiger-Mueller probe. The units are fitted with thin mica windows to permit detection of beta radiation, and aluminum shields may be attached to exclude betas. The detector tubes are halogen-filled to provide a much longer life for training purposes than do their organic-filled counterparts. Geiger-Mueller probes may be inserted into a small, shelved Plexiglas stand for geometry and absorption studies.

Half-Life Demonstrator

A half-life demonstrator has been designed (and built) that permits a dramatic demonstration of radioisotope decay in one laboratory period. The apparatus permits the student to achieve an 80 per cent separation of barium-137 (half life, 2.6 minutes) from its parent cesium-137 (half life, about 30 years) in as little as 30 seconds' time, with no risk of contamination problems. The apparatus has proved extremely valuable in demonstrating half life, parent-daughter relationships, secular equilibrium, and ion-exchange separation.

MEDICAL PHYSICS

Projects in the medical-physics program that are being carried out by the ORINS Medical Division include the following:

Physical Characteristics of the ORINS Linear Scanner

Isoresponse curves are being obtained for the multiple-crystal sensing head of the linear scanner, and these and other physical characteristics are being incorporated into a special report now in preparation.

Clinical Evaluation of the Linear Scanner

Most patients now receiving diagnostic or therapeutic doses of radioisotopes are being studied by means of the linear scanner to determine how the instrument can best be used to furnish desirable clinical information. Records obtained from the linear scans supplement the information obtained from the area scans.

Evaluation of the Area Scintiscan

Area scans are being done where indicated in patients receiving diagnostic or therapeutic radioisotopes, and the information obtained from the scintiscan is correlated with that obtained by other means — diagnostic X rays, for example.

Field-Testing of New Scanning Devices

Scanning instrumentation is developing rapidly and, where possible, the Medical Division is field-testing new devices as they become available. The division expects to test a multiple-point recording hammer, developed by the Physics Division of Oak Ridge National Laboratory, to be used as a print-out mechanism. More effective collimating devices developed at ORNL for use in brain-tumor detection may also be tested by the division.

Thyroid Measurements

The search for more reliable ways of estimating extrathyroidal neck background is continuing as time and opportunity permit. Early thyroid uptakes are probably more informative than those done at any other time, but it is during the early stages that the high neck background presents a particularly formidable problem.

Pulse-Height Spectrometry

The evaluation of clinically oriented pulse-height spectrometers is continuing, particularly in connection with external counting procedures on a patient. Double-isotope studies are also used whenever they are clinically advisable. A handbook discussing the principles and mechanism of a clinical pulse-height spectrometer is in press, and more condensed material of a similar nature has been prepared for use in the Medical Division's training courses.

Oxygen Tensions in Radiotherapy

The exploration of the effect of abnormally high or low oxygen tensions on the radiation sensitivity of tumors is being investigated. This study, still in its early stages, involves the design and construction of special equipment for measuring the oxidation-reduction potentials involved.

Spectral Changes in an External Beam

One of the first steps that must be accomplished in an approach to both external and internal dosimetry is the effect of the body on the spectrum of a beam of radiation. It is possible to present the material as a demonstration, and this has been accomplished at the Medical Division. Complete measurements have been made of the entire spectrum of three isotopes as a beam of radiation passes through the body. One demonstration shows what happens to the spectrum of gamma-ray radiation as the beam penetrates the body; the second demonstrates what happens to the spectrum at various angles of scatter. Both demonstrations have been prepared as three-dimensional models.

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Oak Ridge Institute of Nuclear Studies

Fourteenth Annual Report

OPERATING UNDER CONTRACT

WITH THE

United States Atomic Energy Commission

JUNE 30, 1960

Medical Division

THE year just past might be called a transitional one for the Medical Division, in that, while its basic programs and objectives remained the same, new approaches and new equipment were brought to bear on existing problems, and

section of this report. Work has also continued on implementation of facility space, particularly the D Wing of the old Oak Ridge Hospital that is being turned over to the Medical Division. At the close of the year, the work of alteration was proceeding on counters, area scanners, and other related instruments, is designed to obtain as much of this information as possible from the outside of the patient's body.

The ORINS linear scanner consists of two rows of scintillation crystals with appropriate electronic equipment for pulse-height selection and continuous count-rate recording. One row of detectors is above the table that holds the patient, the other directly beneath it and under the table. Both rows are collimated to "see" only one transverse segment of the body at a time. The table with the patient on it is automatically moved through the sensitive area, and a record is produced that shows the amount of radioactivity at all points along the length of the patient's body.

The linear scanner lies between the area scanner and human body counters in sensitivity and degree of localization of radioactivity. It gives semiquantitative information and good longitudinal definition of areas of activity; better evaluation of areas of diffuse activity, not sharply localized, than the area scanner; and requires only about fifteen minutes of the patient's time.

The information obtained with the linear scanner has many uses. Accidentally ingested radioactivity may be discovered. Radioisotopes formed in the body by accidental neutron irradiation can be assayed. Diagnostic studies with administered isotopes make possible evaluation of the functions of liver, kidney, and other organs. Radioisotopes given for therapeutic purposes can be studied to ascertain that they are properly localized. Finally, with improvements in these detection techniques, there is reason to believe that isotopic cancer-detection studies can be expanded considerably beyond present usefulness.

In its use during the year, the ORINS linear scanner has already revealed unsuspected metastatic lesions from thyroid carcinoma, and patterns of isotope distribution in several diagnostic and therapeutic situations.

ORNL Research Scanner

Since January 1960, a research scanner designed and built at Oak Ridge National Laboratory has been in clinical use at the Medical Division. This is an improved area scanner and has been used primarily in studying patients with thyroid carcinoma and in attempting to detect and localize brain tumor.

With the new research scanner, it is possible to "see" both very large and very small doses of radioactivity, very shortly after administration and at considerable periods after administration. The scanner's sensitivity has been increased so greatly over former models, that it actually presents the problem of over-interpretation of normal physiological findings.

Preliminary work in patients with thyroid carcinoma indicates that this scanner offers a distinct improvement in the facilities for diagnosis and treatment of this disease. It also promises to be a worthwhile addition to the diagnostic procedures available for locating brain tumors. The use of the scanner, following injections of radioactive materials, clearly demonstrated brain tumors in three patients, confirmed by microscopic study of removed tissue. The only known instance of failure to show a tumor when one was present was in a patient with a pituitary tumor.

The new scanner also promises to be of value in the study of tumor in the liver.

Total-Body Irradiation and Marrow-Graft Studies

Further advances in research on total-body irradiation were made at the Medical Division during the year. The program is directed to applications in patients of the important results of animal investigations reported from other laboratories. Studies of the potential usefulness of grafts of bone marrow in patients are an important part of this work.

Analysis has been made of a group of patients with acute and subacute leukemia treated by total-body irradiation at the Medical Division, at relatively high levels, in several cases accompanied by bone-marrow grafts. Results have been varied, for several reasons: 1) Some patients treated have been in unfavorable stages of leukemia, resulting in death before any clear-cut evidence is obtained as to the success or failure of the treatment. 2) Large doses of total-body irradiation alone will produce temporary remissions in certain cases of acute leukemia. In cases that have shown remission after combined treatment, it is difficult to determine the relative importance of each element — irradiation and marrow graft — in the remission.

It was observed that the cells of acute leukemia are often quite radiosensitive, and showed rapid breakdown soon after large doses of irradiation. All leukemic patients showed some degree of bone-marrow hypoplasia after treatment. Some died during this period, after manifestations representing both leukemia and radiation effects. A few developed normal blood formation, but without clearly demonstrating a successful "take" of the bone-marrow graft. Still others developed reactivation of leukemia after only temporary suppression of the leukemia cell count, without any real remission in the disease.

In addition to the high-dose studies, several patients with chronic leukemia and other malignant diseases have been given low doses (50 roentgen midline air dose) of total-body irradiation. None have experienced significant symptoms or adverse effects. Some have shown improvement, with a reduction toward normal of elevated white blood counts; others have shown no definite change. As knowledge and experience are gained at this dose level, higher doses will be given. This type of therapy has been used for many years in the treatment of leukemia and polycythemia; the present study is planned to add newer biochemical and hematologic techniques in evaluation, and to relate the results to effects of higher doses.

In May 1960, the first patients were treated in the Medical Division's newly constructed facility for total-body irradiation. (See picture.) This facility consists of a small room which has eight 500-curie cesium-137 sources, one at each corner, with filters that permit control of the radiation dose rate, and a uniform density at the bed in the center of the room, where the patient lies. Treatment time may vary from a few minutes to several hours.

Thick concrete walls and a labyrinthine entrance confine radiation to the treatment room, and, by a system of mirrors, the patient can be observed during treatment without significant radiation exposure to the observer.

A technician demonstrates the control panel for the ORINS total-body irradiation facility. The mirror at right is one of three in the maze that enables the patient and nurse to see each other at all times.

This new facility provides much more uniform radiation dose to the whole body than previously available improvised techniques using cobalt-60. The new equipment also makes it possible to deliver a given dose over a wide choice of time intervals. The importance of these improvements in flexibility and uniformity of dose is not yet known; it is believed that better control of these factors is one step in allowing a precise study of total-body irradiation.

Amino-Acid Studies

Continuing in conjunction with the foregoing program has been the biochemical analysis of amino acids excreted by humans after total-body irradiation, as a possible index of the level of irradiation.

Previous studies on the victims of the radiation accident at the Oak Ridge Y-12 plant in June 1958 had indicated an increase in excretion of taurine and beta-aminoisobutyric acid, with beta-aminoisobutyric acid as the better indicator of dosage than taurine at higher levels. Subsequent investigations showed increased excretion of these two substances in a leukemia patient who had received 935 roentgens of cobalt-60 irradiation, and in a patient with lung cancer who had been treated with a large dose of nitrogen mustard.

Studies of the excretion of creatine in the Y-12 victims and in patients who had received varying doses of irradiation, at high and low levels, seem to indicate that irradiation does not affect creatine excretion in humans, even when creatine metabolism is abnormal, unless the exposure is to a high dose (as in a patient who received 935 roentgens). It might be possible, therefore, to select victims who had received lethal doses of radiation from those who had received lesser doses on the basis of elevated excretion of three compounds: taurine, beta-aminoisobutyric acid, and creatine. The first two would be elevated at doses similar to those involved in the Y-12 accident — 60 to 300 rad (radiation absorbed dose) — whereas all three compounds would be excreted at higher levels when the exposure dose approached 1000 roentgens.

"Secondary-Disease" Studies

One of the limiting problems in the treatment of irradiation sickness by transplantation of bone-marrow cells is the development of a metabolic disease that appears after recovery from irradiation and that may, but does not necessarily, prove fatal. The nature of this "secondary disease" is unknown, but it is related to a genetic incompatibility between the donor cells and the host. If the metabolic alterations that characterize this disease could be worked out, it is conceivable that treatment would become possible. Since humans are genetically nonidentical, except for certain twins, transplantation of bone-marrow cells might lead to a syndrome similar to the "secondary disease" in animals.

Studies of the distribution of amino acids in plasma and tissue of animals that have been irradiated and given bone marrow have been undertaken jointly by the ORINS Medical Division and the Biology Division of Oak Ridge National Laboratory. This investigation, although incomplete, has already shown that there are changes in the liver. The changes that have so far been found also occur to some degree in mice given genetically identical bone-marrow cells, so they are not related solely to "secondary disease." However, the changes in liver are exaggerated in mice given bone-marrow cells from a different strain, and it is believed that these findings are significant in relation to the metabolic disorder of "secondary disease."

Y-12 Plant Radiation Accident Victims

The men who were exposed to significant amounts of whole-body radiation in the Y-12 plant accident on June 16, 1958, have received periodic medical examinations at the Medical Division. They have continued to work without difficulty, and have remained in good physical condition. Blood counts and bone marrow appear normal and indicate recovery from the profound depression of the bone marrow that was present in their course. These men will continue to receive careful medical observation.

Autopsy Studies After Total-Body Irradiation

During the year, autopsy studies were done on a series of patients, most of whom had advanced acute leukemia not responsive to drug therapy, who died after treatment with total-body irradiation and attempted bone-marrow transplantation at the Medical Division. One phase of an intensive clinical and laboratory evaluation of this treatment is the gross and microscopic study of tissues of ten patients who died at intervals up to 35 weeks after treatment. The exposures, ranging from 210 to 940 roentgens, were usually given in one treatment.

The tissues revealed no harmful consequences of the attempts to transplant marrow. The patients who died relatively soon after treatment showed radiation effects, and evidence of hemorrhage and infection (which may be associated with both radiation and leukemia). Leukemic cells were rare or virtually absent in some. Those who lived more than a month (some of whom had been through a temporary remission of the disease) showed at death typical leukemia without evidence of significant radiation injury. One important observation in this series of cases was the absence of serious radiation damage to the gastrointestinal tract after exposure as high as 940 roentgens.

The number of autopsies that have been carried out throughout the world on persons exposed to total-body irradiation is so extremely small that this work at the Medical Division is particularly important.

Additional Clinical Programs

Several other programs in progress at the year's end and not yet at the point where definitive results are available include studies on body burdens and doses at about the level of the so-called "maximum permissible concentrations" of radionuclides in the intestinal tract; a clinical study of the short-lived isotope, calcium-47, in solving problems in mineral metabolism and bone physiology; and research into the radiosensitivity to tumors and other tissues in relation to the concentration of oxygen.

PRECLINICAL STUDIES

New Isotopes and Methods

The Medical Division continues to study new isotopes and methods for potential medical uses relative to treatment and protection. This emphasis is maintained although the general accent on therapeutic possibilities of radioisotopes as internal emitters has declined — more so because of the rapid success of other experimental aims (diagnostic tests, external measurements, therapy machines, etc.) than to proven failures for internal emitters. New ideas and approaches to enhance the use of radioisotopes as internal sources of irradiation have been scarce since the first efforts with inert colloidal preparations — a factor in the Medical Division's emphasis on this objective.

One objective of the program is the evaluation of radioisotopic preparations for internal use. During this past year, animal studies were made with radioactive yttrium-90 as an internal irradiation source, similar to the manner in which radiogold and radiochromic phosphate have been used. Distribution studies in animals have indicated, however, that the particular preparation of yttrium used in the studies was not sufficiently biologically stable for selective immobilization. Other preparations will be considered.

Earlier studies indicated that certain potentially useful rare-earth radioisotopes (including radioactive isotopes of lutetium, holmium, and yttrium) concentrated in the lymphatic systems draining a particular site of administration. This prompted the recent evaluation of direct intralymphatic administration in experimental animals of radioactive colloidal gold, radiocerium chloride, and radioyttrium chloride. Preliminary results indicated important factors requiring further evaluation: nature of the chemical, dose volume, and administration rate. A proper combination of these factors may afford a practical procedure for intralymphatic administration of radioisotopes.

A small-animal linear scanner has proved a convenient way to screen rapidly the general internal pattern of radioisotopic distribution. Planned studies include the use of radioisotopes whose internal patterns are quite different according to the compound used.

The multiplying uses of nuclear materials produce an increased probability of internal contamination. Many of the contaminants in fission products are uncommon in biological processes; many are heavy metals, difficult to eliminate from the body. Tracer studies with some of these elements indicate that natural excretion occurs mainly during the first few days after administration, corroborating findings at other laboratories with other fission-product metals.

Accomplishments to date on the evaluation of hemodialysis (artificial kidney) as an additional channel of excretion include experience with a relatively broad scope of methods and preliminary application

A college trainee learns to manipulate the controls of the artificial kidney that is used for special radioisotopic studies in the Medical Division's preclinical research program.

to selected radioisotopes. This is not an approach for wide civilian application, but would appear fruitful for special medical problems.

Greater availability of relatively short-lived radioisotopes of medical interest, such as yttrium-90, would greatly promote their usefulness. The Medical Division is field-testing a generator, designed at Brookhaven National Laboratory, to prepare yttrium-90 from its parent, strontium-90, quickly and with minimal strontium contamination. The generator, loaded with 100 millicuries of strontium, yields more than 80 millicuries of yttrium-90 weekly; the product can be separated and prepared for administration in about one hour. The mechanical operation of the generator is excellent; an assay of the product with respect to strontium-90 contamination is incomplete.

Rare-Metals Metabolism

The Medical Division is interested in the metabolism of certain rare metals for three principal reasons: the radioisotopes of potential medical interest they offer; the current expansion in their industrial and commercial availability; the fact that rare-earth radioisotopes account for 25 to 50 per cent of the total radioactivity in fission products at various intervals during the first year of decay.

One phase of the program is concerned with the largely unknown field of the biochemical reactivity of rare metals; another, with the effect of rare metals of unknown physiological role on enzyme systems. Virtually complete at the year's end were studies on the excretory pattern of cerium and yttrium in dogs, and distribution studies of intravenously administered cerium.

The division has found major metabolic effects of certain isotopes to have gonadal, adrenal, and pituitary relationships. Differential localization in the adrenal gland is high and preferential to the cortex; relative distribution to the gonads and pituitary is quite low. It is therefore difficult to correlate present metabolic effects with distribution in the gland itself, or in the rest of the body.

In studies on the microbiological response to various rare metals, especially those represented as fission products, ORINS has investigated the uptake of mixed fission products and of cerium to illustrate the rare-earth component of fission products in bacteria, fungi, and yeasts, because these small, unicellular organisms demonstrate general principles of uptake that will later be applicable to studies with humans. Generally, all organisms showed a prominent concentrating ability of radioactivity, associated with their growth phase; also, the uptake of cerium generally exceeded that of mixed fission products — surprising in view of the wide scope of elemental composition of the latter. The next phase of study is designed to indicate the nature of this upta' ·.

Biochemical Studies — The Rare-Earth Fatty Liver

Toxicity studies of rare earths given intravenously showed acute changes in the livers of rats, with reversions to normalcy in about a week for rats that survived. The change was recognized as acute fatty infiltration, more rapid and intense than other known fatty liver responses. This system is a potential tool of unusual value for fundamental biochemical study of lipid metabolism, as well as for defining the effect of rare metals. ORINS has completed a study on characterization of the rare-earth fatty liver with respect to various influencing factors, and is now undertaking research to define the biochemical mechanism.

The acute metabolic effects caused by certain rare earths in rats and a few other experimental species do not invalidate the potential medical usefulness of their radioisotopes in man. The experimental-animal studies show that only the intravenous route affords any hazard, and that toxicity by all other routes is extremely low. These routes by which toxicity is low are those by which most medical applications would be likely.

TRAINING

During the fiscal year 1958-59, the Medical Division devoted a considerable amount of time and effort to the design, construction, and testing of a group of training devices for use in the courses administered by the division. (See ORINS 13th Annual Report.) The successful development of these devices, as well as laboratory exercises, curricula, and teaching techniques, enabled the division to carry out its program of instructional courses this past year with a relatively small amount of effort and considerable economy of time for the staff members involved.

Ten courses were presented during the year, with a total of 185 participants. They included three sessions each of Preclinical I and Preclinical II, two pathology courses, one autoradiography course, and one course in hematology.

This last course, "Radioisotopes in Hematology," was presented November 16-20, 1959, with approximately 40 participants, and nineteen invited guests who served as faculty, in addition to the regular staff members. Numerous requests for repetition of the course were received, and a number of applicants were not accommodated at the time the course was presented because of space limitations. Although the Medical Division staff is gratified by the response to this special course, the division's main training emphasis will continue to be placed on the regular introductory courses.

Some of the training aids developed for use in these courses have proved so valuable that they have been submitted for publication in the literature, to assist other organizations in their training programs. There has also been an evolution in certain parts of the training courses; these changes, with the addition of new isotope technique procedures and refinements, have been incorporated into the course presentations as their worth has been proved.

Requests have been made that the Medical Division provide intern training and training for medical technicians; such programs are, however, not feasible under present circumstances. It is planned to provide some preliminary training for pathology residents at the division, but the greater part of the pathology-training program will continue to be carried out at the resident's home institution.

Abbott Laboratories offers a student fellowship at the Medical Division, open to medical students during the off quarter of the junior year. During his stay at the division, the student participates in the regular clinical program and becomes acquainted with radioisotope and research techniques. The award this year was given to James Densler of Meharry Medical College, who began his stay at the division in June.

In addition to its regular staff, and those scientists who visited the Medical Division to participate in the training courses, the division continued its program of short- and long-term residencies for "outside" scientists. This year the roster included fourteen resident physicians in attendance for three to four months; two one-year residents in experimental medicine; a one-year postresident in radiology; and four visiting scientists from outside the United States whose terms ran from six months to a year. Further details on these residents is supplied in Appendix III of this report.

APPENDIX III
Medical Division

PUBLICATIONS FROM THE MEDICAL DIVISION (FISCAL YEAR 1959)

Andrews, G. A. "Medical Problems Encountered in the Handling of Radioisotopes. Las Medias de Seguridad contra la Radiacion Observadas en un Laboratorio de Radioisotopos." In "Symposium on Health Physics in Biology and Medicine." Held at the University of Puerto Rico School of Medicine, San Juan, May 26-28, 1958. United States Atomic Energy Commission Report TID-7572, June 1959. pp. 72-91, English edition and pp. 80-90, Spanish edition. No reprints are available but the complete document may be ordered from the Office of Technical Services, Department of Commerce, Washington 25, D. C. Price $2.00.

Andrews, G. A. "Radiation Accidents." In "Fallout." Edited by John M. Fowler. New York. Basic Books, Inc. 1960, pp. 106-114.

Andrews, G. A. "Some General Concepts of the Clinical Use of Radioactive Isotopes." In "Medical Physics," Vol. 3, edited by Otto Glasser. Chicago. The Year Book Publishers, Inc., 1960, pp. 302-306.

Andrews, G. A. and Sitterson, B. W. "Hematologic Effects of the Accidental Radiation Exposure at Y-12." In "The Acute Radiation Syndrome — A Medical Report on the Y-12 Accident, June 16, 1958." United States Atomic Energy Commission Report ORINS-25, April, 1959, M. Brucer, Compiler, pp. 2.1-2.10.

Andrews, G. A., Sitterson, B. W., Kretchmar, A. L., and

Brucer, M. "The Need for Medical Reactors." Talk at the Conference on Medical Uses of Nuclear Reactors, Atlanta, February 16, 1959. Mimeographed, April 1959.

Brucer, M. "The Organization of Scientific Affairs." A summary of remarks made at the Hershey Conference of the Division of Scientific Affairs of the American Medical Association, September 1959. Mimeographed, November 1959.

Brucer, M. "Pushing the Panic Button in Nuclear Medicine." Summary of remarks to the Second Annual Conceptual Symposium, sponsored by the Atomedic Research Center, Inc., Air University, Maxwell Air Force Base, Alabama, March 18-20, 1959. Mimeographed, 1959.

Brucer, M. "A Survey of Brachytherapy." In "Roentgens, rads, and Riddles; a Symposium on Supervoltage Radiation Therapy." Edited by M. Friedman, M. Brucer, and E. Anderson. United States Atomic Energy Commission, 1959, pp. 449-456.

Brucer, M. "Thyroid Radioiodine Uptake Measurement. A Standard System for Universal Intercalibration." United States Atomic Energy Commission Report ORINS-19, June 1959. Available from: Office of Technical Services, Department of Commerce, Washington 25, D. C. Price $3.50.

Brucer, M. "Thyroid Radioiodine Uptake Measurement. A Standard System for Universal Intercalibration." Translated into Japanese by Hirotake Kakehi, M.D. and Teruo Nagai, M.D. Published by the Bunkodo Company, 2 Motofuji-cho, Bunkyo-ku, Tokyo, Japan. Price, 3000 yen.

Darling, D. "The Practicality of Cesium as a Teletherapy Source." In "Roentgens, rads, and Riddles, a Symposium on Supervoltage Radiation Therapy." Edited by M. Friedman, M. Brucer, and E. Anderson. United States Atomic Energy Commission, 1959, pp. 485-489.

Fliedner, T. M., Cronkite, E. P., Bond, V. P., Rubini, J. R., and Andrews, G. A. "The Mitotic Index of Human Bone Marrow in Healthy Individuals and Irradiated Human Beings." Acta haemat. 22, 65-78, 1959.

Glaser, W., Gibbs, W. D., and Andrews, G. A. "The Mechanism of Removal of Rose Bengal from the Plasma of the Rat Determined by Autoradiography and Radioassay." J. Lab. and Clin. Med. 54, 556-561, 1959.

Hayes, R. L. "Chemical Measurement of Integral Dose." In "Roentgens, rads, and Riddles, a Symposium on Supervoltage Radiation Therapy." Edited by M. Friedman, M. Brucer, and E. Anderson. United States Atomic Energy Commission, 1959, pp. 61-68.

Hayes, R. L. "Standard-Man Phantoms." United States Atomic Energy Commission Report ORINS-33, April 1960, 10 pp. Available from: Office of Technical Services, Department of Commerce, Washington 25, D. C. Price $0.50.

Kniseley, R. M. "Important Non-Biological Contributions to Radioisotopic Diagnosis." J. Iowa M. Soc. 49, 619-624, 1959.

Kniseley, R. M. "Panel on Radioisotopes." J. Iowa M. Soc. 49, 741, 1959.

Kretchmar, A. L. "An Alteration in the Excretion of Free Serine in Urine from Irradiated Humans." Nature 183, 1809-1810, 1959.

Kretchmar, A. L. (intr. Gould A. Andrews). "Quantitative Urinary Amino Acid Excretion of Normal Men on Controlled Diets." (abstr.) Clinical Research 8, 84, 1960.

Kretchmar, A. L. "Biochemical Studies." In "The Acute Radiation Syndrome. A Medical Report on the Y-12 Accident, June 16, 1958." United States Atomic Energy Commission Report ORINS-25, April 1959, M. Brucer, Compiler, pp. 4.1-4.4.

Kyker, Granvil C. "Serum Protein Studies." In "The Acute Radiation Syndrome. A Medical Report on the Y-12 Accident, June 16, 1958." United States Atomic Energy Commission Report ORINS-25, April, 1959, M. Brucer, Compiler, pp. 7.1-7.2. plus 8 figures.

Morris, A. C., Jr. "A Linear Scanner for Human Radioisotope Research." United States Atomic Energy Commission Report ORINS-33, March 1960. Available from: Office of Technical Services, Department of Commerce, Washington 25, D. C. Price $0.75.

Papavasiliou, C. G. and Speas, C. J. "Fracture of the Hyoid Bone." Radiology 72, 272-274, 1959.

"Roentgens, rads and Riddles. A Symposium on Supervoltage Radiation Therapy." Edited by Milton Friedman, Marshall Brucer, and Elizabeth Anderson. United States Atomic Energy Commission, 1959, 495 pp. Available from: Superintendent of Documents, Government Printing Office, Washington 25, D. C. Price $3.50.

Ross, D. A. "Discussions held on December 28-30, 1959, at the Headquarters of the International Atomic Energy Agency, Vienna." Mimeographed, January 1960.

Ross, D. A. "Linear Scans." In "The Acute Radiation Syndrome: A Medical Report on the Y-12 Accident, June 16, 1958." U. S. Atomic Energy Commission Report ORINS-25, April 1959, M. Brucer, Compiler, pp. 9.1-9.3 plus 6 scans.

Ross, D. A. "The 'Medical Spectrometer.'" Mimeographed August 1959.

Ross, D. A. "The 'Medical Spectrometer.'" In "Medical Physics," Vol. 3, edited by Otto Glasser. Chicago. The Year Book Publishers, Inc., 1960, pp. 341-345.

Ross, D. A. "Preventive Medicine for Your Counting Equipment." Mimeographed, July 1959.

Ross, D. A. "Visits in England, January 1960." Mimeographed, January 1960.

Simon, N., Brucer, M., and Hayes, R. "Radiation and Leukemia in Carcinoma of the Cervix." Radiology 74, 905-911, 1960.

Sitterson, B. W. "Clinical Report." In "The Acute Radiation Syndrome: A Medical Report on the Y-12 Accident June 16, 1958." United States Atomic Energy Commission Report ORINS-25, April 1959, M. Brucer, Compiler, pp. 1.1-1.32.

Snyder, F., Cress, E. A., and Kyker, G. C. "Liver Lipid Response to Intravenous Injection of Rare Earths in Rats." J. Lipid Research 1, 125-131, 1959.

Snyder, F., Cress, E. A., and Kyker, G. C. "Rare-Earth Fatty Liver." Nature 185, 480-481, 1960.

Snyder, F. and Stephens, N. "A Simplified Spectrophotometric Determination of Ester Groups in Lipids." Biochim. Biophys. Acta 34, 244-245, 1959.

Snyder, F., Stephens, N., Gerst, L., and Kyker, G. C. "The Rare-Earth Fatty Liver: Plasma Free Fatty Acids." Fed. Proc. 19, 229, 1960 (abstr. 148.5).

Steffee, C. H. "Histopathologic Effects of Rare Earths Administered Intraperitoneally to Rats — A Preliminary Report." A. M. A. Arch. Indust. H. 20, 414-419, 1959.

ISOTOPES USED BY MEDICAL DIVISION

Arsenic-74	12.2	mc
Gold-198	1760	mc
Calcium-47	3.59	mc
Cerium-Praseodymium-144 (P)	115	mc
Chlorine-36 (P)	10	mc
Cobalt-57	0.00076	mc
Chromium-51	5	mc
Cesium-Barium-137 (P)	50	mc
Iron-59	1	mc
Iron-59 (P)	0.5	mc
Fission Products	15	mc
Iodine-131 Diodrast	1	mc
Iodine-131 Oriodide	4,608	mc
Iodine-131 Radiocaps	28.53	mc
Iodine-131 Rose Bengal	15.75	mc
Iodine-132	150	mc
Lanthanum-140 (P)	190	mc
Sodium-22	0.5	mc
Phosphorous-32	280	mc
Raolein	0.55	mc
Iodine-131 Risa	51.25	mc
Sulfur-35 (P-1)	10	mc
Thulium	5	mc
Yttrium-90	40	mc
Triomet	0.50	mc

ORINS HOSPITAL PATIENT DAYS

July	568
August	415
September	553
October	568
November	477
December	295
January	318
February	382
March	389
April	507
May	449
June	550
Total Patient Days	5471
Average Per Month	455.11
Average Per Day	12.2

MEDICAL DIVISION COURSES

Preclinical II — August 3-7, 1959 .... 12 participants
Pathology — September 7-11, 1959 .... 14 participants
Preclinical I — October 5-9, 1959 .... 19 participants
Hematology — November 16-20, 1959 .... 37 participants
Preclinical II — December 7-11, 1959 .... 20 participants
Preclinical I — January 25-29, 1960 .... 20 participants
Pathology — February 22-26, 1960 .... 19 participants
Preclinical II — March 21-25, 1960 .... 16 participants
Preclinical I — May 23-27, 1960 .... 20 participants
Autoradiography — June 20-24, 1960 .... 8 participants

VISITING SCIENTISTS

Asri Rasad, M.D. .... University of Tennessee
Memphis, Tennessee

Yoichiro Umegaki, M.D. .... Shinshu University Hospital
Matsumotoshi, Japan

Toruo Nagai, M. D. .... National Institute of Radiological
Sciences, Kurosuma-cho, Chiba-shi
Chiba-ken, Japan

Hiroshi Saito .... Department of Internal Medicine
Nagoya University
Nagoya, Japan

POSTRESIDENT IN RADIOLOGY

Jose Briones, M.D. .... Department of Radiology
University of Tennessee Memorial Hospital
Knoxville, Tennessee

RESIDENTS IN EXPERIMENTAL MEDICINE

Flora Pascasio, M.D. .... Kings County Hospital
Brooklyn, New York

Francis T. Oda, M.D. .... University of Maryland
Baltimore, Maryland

RESIDENT PHYSICIANS

Stefan Issarescu, M.D. .... New England Deaconess Hospital
Boston, Massachusetts

Walther T. Weylman, M.D. Massachusetts General Hospital
Boston, Massachusetts

David Foxman, M.D. .... Cleveland Metropolitan Hospital
Cleveland, Ohio

Robert D. Hieber, M.D. .... Boston City Hospital
Boston, Massachusetts

Hsing-Lin Liu, M.D. .... Cook County Hospital
Chicago, Illinois

Freidoun Eskandari, M.D. .... Cleveland Metropolitan Hospital
Cleveland, Ohio

Robert Dingle, M.D. .... Boston City Hospital
Boston, Massachusetts

William T. McCoy, M.D. .... Massachusetts General Hospital
Boston, Massachusetts

John B. Little, M.D. .... Massachusetts General Hospital
Boston, Massachusetts

Elwin W. Donnelly, M.D. .... Massachusetts General Hospital
Boston, Massachusetts

Sigmundur Magnusson, M.D. .... Boston City Hospital
Boston, Massachusetts

Murray L. Janower, M.D. .... Massachusetts General Hospital
Boston, Massachusetts

Yosh Maruyama, M.D. .... Massachusetts General Hospital
Boston, Massachusetts

Juan Fayos, M.D. .... Swedish Hospital
Seattle, Washington

MEDICAL DIVISION CLINICAL CONFERENCES — 1959

July 2: A report of the meeting of the Society of Nuclear Medicine, Chicago — R. L. Hayes, D. A. Ross, G. C. Kyker, G. A. Andrews, M. Brucer.
Report on biomedical directors' meeting — C. S. Shoup.

July 9: Idiopathic thrombocytopenia purpura. Lymphadenopathy and pleural effusion (diagnostic problem) — Clinical staff.

July 16: Changes in liver composition — A. W. Lawrence.
Lipid distribution studies — Fred Snyder.

July 23: Polycythemia with jaundice and weight loss (case presentation with autopsy findings) — Clinical staff.

July 30: Two cases of anemia of unknown etiology — Clinical staff.

August 6: Diagnostic uses of radioiodine — A. L. Kretchmar.

August 13: Discussion of laboratory exercises in preclinical courses — M. Brucer, R. M. Kniseley, clinical staff.

August 20: Setting-up procedures for scintillation equipment — D. A. Ross.

August 27: Oxidative enzyme studies in normal and cerium-treated rat livers — F. D. Baker.
Fission-product and cerium uptake by various microorganisms — G. T. Johnson.

September 3: Two patients with leukemia and unusual pulmonary lesions — Clinical staff.

September 10: Fission-product and cerium uptake by various microorganisms — G. T. Johnson.

September 17: Iron kinetic studies with Fe-59 — W. N. Tauxe.

September 24: Clinical pathological conference — Clinical staff.

October 1: Dosage in clinical radiotherapy — F. Comas.

October 8: Two cases of hyperthyroidism — Clinical staff.

October 15: Portal hypertension with esophageal varices and hypersplenism (discussion of surgical treatment) —F. Oda.

October 22: The use of metacorten in the treatment of hematologic disorders — R. D. Hieber.

October 29: An unusual case of anemia and hepatosplenomegaly with autopsy findings — Bill M. Nelson.

November 5: Preliminary studies with calcium-47 — G. I. Gleason, G. C. Kyker, D. A. Ross, Flora Pascasio.

November 12: Problems in nuclear medicine (Midget Exhibit F-2) — M. Brucer.

November 19: Total-body irradiation — B. W. Sitterson, G. A. Andrews.
Discussion—E. Donnell Thomas, C. C. Congdon, et. al.

December 3: Lethal and leukemogenic effects of irradiation —D. J. Mewissen.

December 10: Diagnostic uses of radioiodine — A. L. Kretchmar.

December 17: Whole-body counters — D. A. Ross.

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January 7: A patient with Hodgkin's disease and bilateral pleural effusion, illustrating a change in the morphology of the neoplasm — Clinical staff.

January 14: Plasma-free fatty acids and fatty-liver infiltration — Fred Snyder.

January 21: 50 r total-body irradiation in hematologic disorders (plans and preliminary results) — Clinical staff.

January 28: Therapeutic uses of radioiodine — Clinical staff.

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February 4: Modification of radiation response — F. Comas.

February 11: Modification of radiation response (continued) — F. Comas.

February 18: Testing for effectiveness of the training program — R. M. Kniseley.

February 25: Whole-body counting in thyroid disease — C. C. Lushbaugh.

March 3: Snatches from the Chalk River meetings — G. C. Kyker.

March 10: Porphyrins and whole-body irradiation — R. L. Hayes.

March 17: Case illustrating diagnostic, therapeutic, and investigative uses of isotopes — Clinical staff.

March 24: Tests for thyroid function — A. L. Kretchmar, B. W. Sitterson, G. A. Andrews, R. M. Kniseley, et. al.

March 31: Polycythemia with terminal myeloproliferative disorder — Clinical-pathological staff.

April 7: Two diagnostic cases — Clinical staff.

April 14: Whole-body doses (past, present, future) — A. C. Morris, Jr., D. A. Ross, M. Brucer.

April 21: Autopsy findings in ten patients treated with total-body irradiation for leukemia — Bill M. Nelson, C. H. Steffee.

April 28: Enlargement of liver in irradiated mice treated with bone marrow — A. L. Kretchmar.

May 5: Research scanner in clinical use: Hot spots . . . but what — Clinical staff.

May 12: Liquid scintillation counting — Fred Snyder.

May 19: Metastatic carcinoma with autopsy findings — Bill M. Nelson, clinical staff.

May 26: Two cases of thyroid disease for possible iodine-131 therapy — Clinical staff.

June 2: Preliminary radioisotopic studies of the artificial kidney — Asari Rasad.

June 9: Preliminary report on brain scanning program — F. Oda, C. C. Harris, J. E. Francis, Jr.

June 16: Review of some effects of total-body irradiation in human beings — R. M. Kniseley.

June 23: Absorption and excretion of amino acids — R. C. Baldridge.

June 30: A nerve growth promoting protein — Stanley Cohen.

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Oak Ridge Institute of Nuclear Studies

Fifteenth Annual Report

OPERATING UNDER CONTRACT

WITH THE

United States Atomic Energy Commission

JUNE 30, 1961

Medical Division

STUDIES on the effects of radiation in man have continued to occupy a prominent place in the clinical research program during the past year. The new total-body irradiation facility was completed and this permits giving a more uniform radiation dose over a wide range of dose rates. Emphasis has shifted from attempts to obtain successful grafts of bone marrow in patients given large doses of total-body irradiation to studying the effects of small doses of radiation given to the whole body in various diseases. This program has been broadened to include immunological studies by the addition of an immunologist to the staff in midyear. Special studies of the effects of local port irradiation on normal bone marrow are being done in patients receiving radiation therapy for nonhematologic diseases.

Applications of radioisotopes in the study and treatment of hematologic disorders in general continues to be of great interest. Special projects started in this area during the year include studies on isotopically labeled blood platelets and plasma cells.

The long-range programs pertaining to diagnostic and therapeutic uses of internal radioisotopes have been pursued. In addition to their research value, these programs give basic training for resident physicians. They also provide the basis for most of the scanning, which constitutes a program in itself. Continual attempts have been made to improve scanning equipment, techniques and interpretation, and to extend the applications of this procedure.

The outpatient service has grown considerably both in scope and number of patients.

CLINICAL STUDIES

Total-body Irradiator

The Medical Division of the Oak Ridge Institute of Nuclear Studies has been making use of the specially designed total-body irradiation facility that was completed last year. This instrument employs eight sources of cesium-137 (an isotope with a long half life), so arranged that a uniform radiation dose can be given to the whole body of a patient. It is also possible to vary the dose per minute over a rather wide range in order to determine whether the effects of a given dose are dependent on the speed with which it is delivered.

ANIMAL STUDIES. The large, uniform radiation field produced by this instrument makes it possible to irradiate animals without confining them in small containers. Information derived from animal studies can be correlated with that derived from studies of patients, with assurance that the irradiation was delivered under identical conditions. It is true, of course, that in small animals the size of the body allows much greater relative penetration of the radiation; however, with the high energy of cesium-137, this difference in effect is not so pronounced as it would be with lower-energy radiation.

DOSIMETRY. Measurements are being made on the radiation doses the new irradiator produces in tissues. The exposure in air can be easily measured and is known to be uniform over the whole area in which the patient lies; however, the dose to the deeper organs depends somewhat on the size of the patient, the thickness of tissue between the radiation sources and the area of interest.

To measure these doses at various depths, three models or "phantoms" were made with multiple compartments to represent the size and approximate di-

Staff members of the ORINS Medical Division are shown preparing a series of dosimetry studies in the division's total-body-irradiation facility, using a "phantom" to represent a patient's body.

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mensions of the various parts of the body for a small, a medium-sized, and a large patient. Measurements have been made in these phantoms by means of electronic dosimeters. In addition, the average doses for whole zones of the body are being measured with chemical dosimeters dissolved in a liquid medium representing tissue.

TREATMENT OF PATIENTS. For many years, low-dose irradiation of the whole body has been used in the treatment of polycythemia and chronic leukemia. Studies are now in progress at the Medical Division to quantitate the effects of such treatment. Carefully standardized delivery of the irradiation and systematic collection of data may add to knowledge already reported in the literature. It will also be possible to make comparisons with radiation delivered by other means —for example, with internal radioisotopes.

At higher doses, efforts are being made to treat other diseases not ordinarily treated in this way. Patients with acute leukemia and widespread malignancies of various types are in this study. Marrow-graft studies are a major subject for investigation. The achievement of successful marrow grafts in human patients has proved exceedingly difficult. Temporary remissions in acute leukemia have been produced by irradiation and administration of marrow from donors of different genetic constitution. It is now believed that in most of these instances there was no true survival of the graft and the clinical benefit is attributed to the irradiation alone. Although this is a disappointing observation from the point of view of the attempted marrow graft, it is of value to know that irradiation alone can have this effect on acute leukemia. It is an effect that appears similar to that produced by antileukemic drugs such as Methotrexate and 6-Mercaptopurine.

Total-body Irradiation

IMMUNOLOGIC STUDIES IN PATIENTS. Antibodies are normally produced as a part of the body's protective system against microorganisms and foreign cells. This immune mechanism, although protective, also prevents the acceptance of donations of tissue from other persons. Animal studies and clinical observations have demonstrated that total-body irradiation will depress the ability to produce antibodies. Knowledge about the exact effects of irradiation on this mechanism is important as a part of tissue-graft attempts and as a basis for combating infection in heavily irradiated patients. At the Medical Division, a program has been initiated to define as clearly as possible the immune mechanism of the irradiated patient. Responses of patients treated by total-body irradiation are assayed by selected immunologic techniques. It is also planned to analyze the antibody-forming potentialities of cells obtained from patients when these cells have been subjected to certain types of chemical or radiation exposure.

MARROW-GRAFT LABELING STUDIES. One of the problems confronting workers in attempted marrow grafts is the difficulty in determining the fate of the injected material in assaying a graft "take." At the Medical Division, two patients were transfused with bone marrrow that had been labeled with radioactive thymidine. It was possible to detect these tagged cells in the bone marrow and in the peripheral blood for several days, and there was evidence that these cells had shown some proliferative capacity after injection. By ten days no cells were any longer detectable, and the method proved to be laborious, with only a rare labeled cell being available for study.

BIOCHEMISTRY OF TOTAL-BODY IRRADIATION IN PATIENTS. Biochemical effects of irradiation have been studied to develop a method for determining doses in radiation accidents. Such knowledge will lead to fuller understanding of radiation injury and its treatment. The intentional use of total-body irradiation in the treatment of leukemia and cancer may have increased value if biochemical effects are clearly understood.

Further studies of the effects radiation has on excretion of amino acids in the urine have been pursued at the Medical Division. Assays were performed on the urine from six persons exposed to an X-irradiation accident at the so-called "Lockport (N.Y.) incident." These data were added to the earlier information collected from study of the taurine and beta-aminoisobutyric acid excretion in the urine of the five men exposed in an accident at the Oak Ridge Y-12 plant in June 1958, and in a man exposed to a lethal dose of radiation at Los Alamos in 1958. Unfortunately, in the Lockport group, early samples of urine were not available, hence, the previously noted early increased levels of beta aminoisobutyric acid excretion were not confirmed. Nevertheless, the taurine excretion study did support earlier observation. Correlation was observed between the estimated dosage and the amount of taurine excreted in the four- to six-day postexposure time interval.

The effect of total-body irradiation on the excretion of taurine and beta-aminoisobutyric acid has also been studied at the Medical Division in patients with leukemia. An early excretion of increased amounts of beta-aminoisobutyric acid is observed, with a progressive decrease to levels below pre-irradiation levels. A similar observation was obtained after a large dose of nitrogen mustard, an anticancer drug. The effect of irradiation on taurine excretion in the leukemic patients studied thus far is not uniform. The evaluation of the data is complicated and depends in part on the levels of taurine excretion before irradiation, which in turn are dependent on the ingestion of meat protein in the diet. In contrast to irradiation, nitrogen mustard therapy in one patient produced an immediate elevation of taurine excretion, which was maintained for a period of ten days.

BIOCHEMICAL CHANGES AFTER BONE-MARROW GRAFTS IN ANIMALS. It has been observed that the liver enlarges in animals given a bone-marrow transplant following lethal amounts of irradiation. Changes are greater in animals given homologous cells (from unrelated donors) than in animals given genetically identical cells. This alteration in liver size may play a significant role in "secondary disease," the disorder that causes delayed death in animals given foreign marrow after irradiation. This secondary disease has assumed great importance as the main obstacle to successful marrow grafts in experimental animals and may prove to be the greatest limitation in human marrow-graft attempts. At the ORINS Medical Division and Oak Ridge National Laboratory, a joint study was undertaken to see whether these changes in liver weight were correlated with alterations in splenic weight and to investigate the biochemistry of secondary disease. The finding that a correlation is present supports the idea that the changes in the liver size and aspects of its chemistry are related to hemopoiesis (formation of blood cells). The results suggest that the liver synthesizes precursor material for tissue components and that this production of precursor material is not restricted to cells of the hemopoietic system. Chemical assay of the total nitrogen content of these livers was determined and increases of nitrogen content were observed in animals given isologous (identi-

anemia associated with these diseases is obtained from diagnostic studies with chromium-51 and iron-59. The degree of involvement of the liver and spleen can sometimes be determined by radioisotope studies and scanning techniques. Two specific problems in these patients have been the subject of research studies—hypersplenism and surgery.

HYPERSPLENISM is a condition in which the spleen is involved by the chronic blood disorder in such a way as to add to the severity of the disease. The spleen may act to destroy red cells or reduce the number of white cells and platelets (clotting elements) in the blood. In such situations, removal of the spleen would be desirable, but because of the presence of the chronic illness, surgery has an added risk and may not be justifiable. At the Medical Division, irradiation of the spleen in doses higher than those usually used has been applied in these cases, preceded and followed by careful laboratory tests to indicate the effect. The treatment in most patients has failed to control the hypersplenic state, although it has sometimes been beneficial in other ways to alleviate symptoms.

SURGERY is often contemplated in these patients with chronic blood diseases, not only removal of the spleen for hypersplenism but other needed operations, which may or may not be related to the original disease. A review has been made of the results of such operations. A rather high incidence of postoperative complications has been noted. Certain principles in deciding on surgery have been set down. In general, these patients tolerate operations reasonably well, and when surgery is needed it usually should not be prohibited because of the presence of a chronic blood disease.

TELETHERAPY. The development and use of radioactive isotopes for teletherapy is a major interest of the ORINS Medical Division. The great improvement in these and other instruments for delivering radiation from outside the body has added materially to potentialities for successful treatment of certain types of can-

A regular Medical Division staff member confers with a visiting scientist from Thailand on a plan of teletherapy treatment for a patient in the ORINS hospital.

standard X-ray studies. There is an opportunity to obtain specific information at the time of operation, and surgeons are being urged to describe carefully the tumors they find unremovable. Sometimes small, harmless, metal clips that can be seen with X rays are left inside the body to mark the limits of the tumor. For a group of patients treated for carcinoma of the urinary bladder at Oak Ridge, an abdominal operation is done for the purpose of determining the size and location of the tumor and its extensions. Up to the present time, eleven patients have been treated according to this plan. It is too early to determine the results and it is expected that several years will be required to build up an adequate series of cases and to observe the outcome.

RADIOIODINE IN CANCER OF THE THYROID. The use of iodine-131 in the treatment of cancer of the thyroid is constantly changing, because of new equipment and new knowledge. After the enthusiasm that followed the first discovery that the isotope treatment caused dramatic benefit in certain cases, there was a period of disillusionment associated with the discovery that only a relatively small number of patients with the disease would show an impressive concentration of the radioisotope in the areas of tumor.

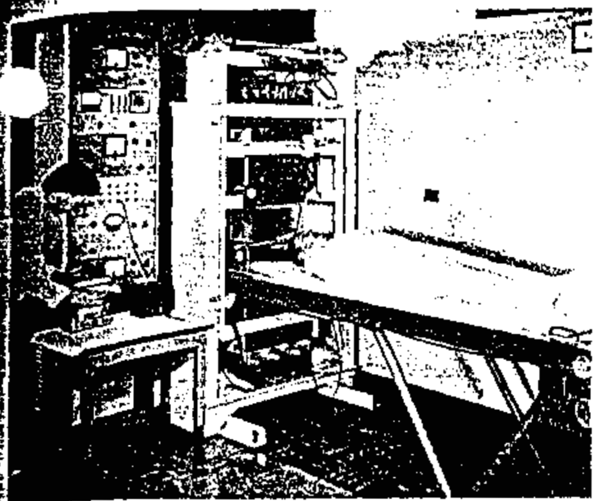
During the past six or eight years improved methods have made it possible to use radioiodine as a valuable adjunct to surgical therapy. Surgery is effective for most cases of carcinoma of the thyroid, but in the past a great limitation has been that surgeons could not determine the extent of the tumor-spread in lymph nodes of the neck and upper chest. Even operations that remove large amounts of normal tissue often leave nodules of tumor in adjacent areas. Studies at the Medical Division of the Oak Ridge Institute of Nuclear Studies have shown that radioiodine will help to locate these areas of cancer, and allow their surgical removal in a rather high percentage of cases. The improvements in detection have resulted from much better radioisotope scanning equipment and the use of larger test doses. The most sensitive studies are often made several days after the isotope has been given. Another important part of this program has been the use of a surgical probe counter for detection of small functioning tumors at operation. Several more years will be required before final evaluation can be made of this approach to therapy. In these patients treated effectively so far, it is possible that areas of tumor will be revealed that have completely failed to take up the radioisotope, and have thus been allowed to persist in spite of the best observation. The study has already shown conclusively, however, that many patients treated by conventional and rather radical surgery, without benefit of radioiodine studies, are inadequately treated.

Isotope Localization Studies

All diagnostic and therapeutic applications of internally administered radioisotopes are based upon knowledge of the distribution and localization of the material in the body. Essential requirements to gathering such information are that the doses administered must not be required to remain still for inordinately long periods while being studied, and that the number of blood samples obtained must not be unreasonably large. Although a sample of an isotope in a test tube can usually be measured accurately with ease, detection and measurement of an isotope inside a patient present diffculties. The dynamic state may create continuous change in isotope distribution. Furthermore, varying amounts of the radiation are absorbed as it passes from the body and thus the measurements made on the outside depend on the thickness and type of tissue between the isotope and the detector.

Radioisotope scanning techniques have been a major area of research effort at the Medical Division. A linear scanner has proved exceedingly useful in showing the distribution of isotopes in relation to the long axis of the body. It does not give any indication of the location of the radioactivity in the lateral dimension, but yields data more nearly quantitative than that obtained from area scanners. Since the linear scanner assays the whole body quickly, it is of value in studying total distribution rather than localization within a small area.

Further studies at the Medical Division with the improved area scanner, developed at the Oak Ridge



The linear scanner used at the Medical Division shows the location of isotopes administered for diagnostic and therapeutic purposes in relation to the long axis of the body at various intervals, after oral administration of the radioisotope.

National Laboratory, have yielded interesting and valuable information. Most of its use has been in patients with carcinoma of the thyroid. Small areas of poorly functioning tumor can now be located. Some of these have been found in patients who, on the basis of the best studies previously available, had been thought to be entirely free of residual tumor. Along with showing areas of tumor or normal thyroid tissue, the improved sensitivity of the scanner has made it possible to study other areas of normal concentration of iodine in the body. Most of these were never noted in studies with the equipment available earlier. Some of them cause trouble in diagnosis of areas of tumor. Zones of activity in the region of the mouth and nose are believed to be associated with salivary and other glandular secretions. The salivary glands themselves are sometimes seen clearly. Another zone of normal activity forms a linear pattern low in the neck; this may be associated with the trachea or esophagus. The nonlactating breast is sometimes seen to show iodine-131 concentration. Somewhat variable areas of concentration have been seen in the mediastinum and lungs. Radioiodine is often seen in the intestinal tract and a faint concentration in the liver may be noted.

This new scanner has given improved views of the size, location, and function of the liver. Evidences of tumors in the liver are sometimes seen, but only large lesions are reliably detected. The spleen can be shown with intravenously administered radioactive colloids, and occasionally this yields information of diagnostic value.

The instrument has also served for studies of brain tumors. A total of 36 patients has been studied, with positive findings in nine. Of these, histological confirmation has been made in seven and surgery has been refused by two. Of the patients with normal scans, three are known to have some intracranial abnormality; only one of these had a tumor.

Tracer Techniques in Medicine

HEMATOLOGY. Clinical evaluation of blood disorders and dynamics of blood-cell formation has been greatly advanced by radioactive tracers, perhaps second only to the remarkable progress provided by iodine-131 in the study and treatment of thyroid disorders. Various techniques for evaluating red-cell survival time, blood volume and red cell mass, and iron absorption and utilization have been adopted to study patients with disorders of blood-forming organs. During the past year one special project at the Medical Division of the Oak Ridge Institute of Nuclear Studies has been the determination of the life span of platelets, the small structures in the blood that play a part in clotting. These studies have been done both in patients with normal and those with abnormally high levels of circulating platelets. The patient is given sulfur-35 injections and some of the isotope is incorporated into megakaryocytes (cells of the marrow that produce platelets). The platelets subsequently formed contain the radioactive label and the amounts of radioactivity appearing in the circulating platelets over a period of days allow a curve to be plotted that indicates the life span of these structures.

Effects of Local Radiation on the Bone Marrow

Extensive studies have been carried out in animals to define the nature of radiation damage to blood-forming tissues, the response of these tissues, and their capacity to regenerate. Less complete data have been gathered in human beings, although valuable observations have been made on the rare radiation accident victims, and patients treated with total-body irradiation.

The knowledge of effects of local or "port" irradiation on blood-forming tissues is incomplete. Some patients develop depression of white- and red-cell numbers after radiation directed to a small part of the body.

At ORINS, marrow of patients being treated for certain cancers has been studied before and during the course of radiation therapy, and during the recovery phase. The pattern of marrow depletion under these treatment sites has been compared with unirradiated sites by histologic sections, differential counts, iron stains, and the ability of the cells to take up radioactive thymidine, a precursor of DNA (deoxyribonucleic acid). The depletion of the usual white-cell and red-cell precursors occurs fairly early in the course of the radiation therapy, which usually is carried out over a period of several weeks to obtain a cancer-killing dose.

The appearance of regeneration is less uniform. In some patients, increased iron deposits develop in the irradiated sites.

Y-12 Accident Victims

Examinations of the patients from the Oak Ridge Y-12 electromagnetic-plant radiation accident of June 16, 1958, have been conducted on an outpatient basis at intervals of approximately six months. In general, the men have remained well, and have continued to work full time. There has been slowly progressive decrease in indications in the men of fatigue, muscle stiffness, nervousness, and insomnia, although they still persist in degrees varying from patient to patient, and without correlation with the amount of radiation received.

PRECLINICAL STUDIES

New Isotopes and Methods

An investigation was made at the Medical Division on the artificial kidney as a possible adjunct to the treatment of internal contamination with radioisotopes. The artificial kidney is a device that is used in treating patients with kidney failure. A stream of blood bypasses through the instrument where certain substances are removed by dialysis, and then is returned to the body. After the accidental intake of a radioisotope, this device might offer some assistance in early removal of the unwanted material. In the studies done in dogs at Oak Ridge, it was found possible to remove significant amounts of some soluble radioisotopes (sodium-24, iodine-131) but cerium-144 was not effectively removed even when large amounts of a chelating agent were used to bind the isotope and keep it in a potentially removable form.

The specially designed yttrium-90 generator produced at the Brookhaven National Laboratory was found to be practical and useful in tests at the division. The device allows preparation of the yttrium from its parent, strontium-90. Because of the long half life of the parent isotope, the generator, once loaded, makes the yttrium isotope available for a long period without reloading, thus allowing continuous availability of this isotope which has considerable value in investigational and clinical work.

Nuclear Minerals Metabolism

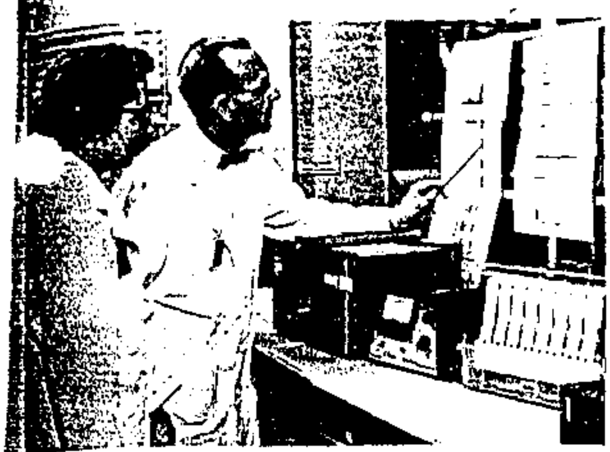
The elements of the lanthanide series have continued to be the subject of detailed investigations at the Medical Division. These substances are important because relatively large amounts are present in fission products. This means that they may constitute a possible hazard for accidental human ingestion. On the other hand, it means that they are available in quantity for possible useful applications. Some of them have been shown to have potential value for medical applications.

Tracer measurements of a wide range of oral doses have shown no appreciable gastrointestinal absorption.

Cerium is as toxic as, or more so than, others in this series, and when given intravenously to rats in stable form, causes acute metabolic disturbances, particularly temporary fatty infiltration of the liver. This acute change is associated with a sharp reduction in food intake and causes death in a small percentage of animals. In the rest, recovery appears complete within a week. During the past year studies have been carried forward on the mechanisms of production of this liver lesion. The endocrine status of the animal was found to play a large role in the occurrence of the liver changes. Adrenalectomy, hypophysectomy, thyroidectomy, and alloxan diabetes will all prevent or greatly reduce the amount of fatty infiltration of the liver after a standard dose of cerium. Distribution studies in which radioisotope tracers were used showed that these alterations in effects related to hormonal state were not based upon alterations in the distribution of the cerium.

There is much evidence to indicate the prominent role of plasma proteins in complexing and solubilizing various elements among heavy nuclear minerals. Paper-electrophoretic studies confirm that there is an association, but they .re not an adequate source of evidence to indicate specific protein metal complexes. Preliminary results from the use of microchemical procedures have indicated an effect on blood-sugar levels which may be of significance in the explanation of the metabolic effect of cerium and certain other lanthanons.

Chemical factors also play an important part in the production of the rare-earth fatty liver. The routine procedure calls for administration of the element as



Two Medical Division staff members are shown examining results of electrophoretic separation of serum proteins, as part of the Division's preclinical research program.

the chloride in a saline solution slightly acidified for stability. If the pH is raised before administration, fatty liver does not occur. Administration as the previously prepared versenate also gives protection, but the administration of versene immediately after the cerium fails to protect. A less stable complex, cerium citrate, also causes fatty liver like the chloride. Changes in the characteristic spectrum of selected lanthanons caused by the presence of various biochemicals that were tested, gave evidence of interaction in dilute solutions.

Preliminary measurements of subcellular distribution cerium in liver have included nuclear, mitochondrial, submicroscopic, and dissolved fractions prepared by centrifugation. The dose of cerium that causes fatty infiltration is distributed among each of the four fractions; strictly duplicable results are difficult to obtain, but the data suggest some translocation from the coarser to the finer fractions during the more intense phase of the fatty infiltration.

The inhibition of enzymes by lanthanons representative of those which do and those which do not produce acute fatty liver was observed for relatively simple enzyme systems (hydrolysases). Evidence of interaction with the enzyme protein is suggested by the increased inhibition that occurs when the enzyme is preincubated with the metal at a given concentration.

Although the fatty liver produced in rats by intravenous cerium is temporary, the element tends to stay in the liver for a long period of time. Furthermore, it can be given repeatedly and the temporary fatty liver response again produced. As many as 75 repeated doses (2 mg cerium per kg of rat) have been given over a space of three or four months. Localization in liver occurs as for the single dose and a large total liver content builds up, suggesting the possible use of nontoxic elements in this series for radiographic delineation of the liver.

Lipid Metabolic Studies

Studies of lipid metabolism were undertaken to throw some light on the acute metabolic disturbance caused by various nuclear minerals. The rare-earth fatty liver, further characterized by lipid measurement, has become an extraordinarily useful tool for the study of lipid metabolism, since it is characterized by periods of rapid accumulation in one organ and subsequent removal. The speed and intensity of fatty infiltration due to cerium and certain other lanthanons are dramatic, reaching three times the normal level of total liver lipids with 48 hours, followed by complete recovery during three or four additional days. Chromatographic separations (silicic acid chromatography) have shown that the rapid changes in lipid composition are attributable to neutral fat. Subfractions of the phospholipid fraction of total liver lipids may show relative changes of metabolic significance but the gross effect is due to triglyceride. Measurements both on the intact animal and at the cellular level concur to suggest an inhibited utilization of lipid. More impressive evidence from measurements of individual fatty acids supports the conclusion that mobilization of adipose fat, which is normally found at various other places in the body, is a major factor in explaining the increased liver lipids. Gas chromatography for the measurement of individual fatty acids qualitatively and quantitatively has found extensive use in these studies. The fatty acid composition of liver fat and of adipose fat are distinctly different in the rat, oleic acid normally predominating in one and stearic acid in the other. During the development of fatty infiltration from cerium the oleic-stearic acid ratio of liver fat tends to invert, to become like that of adipose fat. Concurrent changes in the fatty acid composition of plasma also give supporting evidence that mobilization is a major factor in the explanation. Various other biochemical stresses causing fatty infiltration have been compared with the rare-earth fatty liver by the same methodology.

Total-body Irradiation Effects on Lipids

Acute total-body irradiation is reported by various laboratories to increase the total plasma lipids of various experimental animals. Relatively little information is known about specific changes of individual fatty acids. Only recently, experiments were begun at the Medical Division of the Oak Ridge Institute of

Nuclear Studies to study the effects of total-body irradiation on the plasma lipids of the rat. Twenty-four hours after exposure to 840 r, distinct changes are seen in the fatty acid profile of plasma lipids. In the normal rat, fatty acids with 18 carbon atoms compose practically all of the plasma lipids. After irradiation, significant quantities of various short chain fatty acids appear, the normal fatty acids are relatively decreased, and there also appear to be abnormal fatty acids of longer chain length. Preliminary experiments on brain lipids following similar doses to the head only show changes that resemble those in plasma lipids after total-body irradiation. These findings are of special interest both for their fundamental significance, for the possible evaluation of irradiation dose after exposure, and for comparison with parallel studies of patients receiving total-body irradiation as therapy for leukemia.

Radiation Effects on Hemoglobin Formation

Total-body irradiation is known to have profound effects on red cell formation. At the Medical Division an investigation has been initiated on the early steps of hemoglobin synthesis, with emphasis on heme precursors. (Elevated protoporphyrin has been reported in animal radiation studies.) A first step was the investigation of methods for separation and analysis of urine porphobilinogen (PBG) and delta-aminolevulinic acid (ALA). Present methods proved too insensitive for levels involved in clinical chemical measurements, and preliminary work was done on large-scale, ion-exchange separation of the compounds by pH fractionation.

TRAINING

Training activities continue to be an essential activity of the Medical Division, and may be classified in three groups: resident and fellowship training, qualification courses and special seminars, and miscellaneous. All are important in the division's mission to develop, collect, and disseminate information on the medical uses of radioisotopes.

Resident and Fellowship Training

Ten short-term residents from several institutions averaged three to four months in training. Also, two third-year medical students were here under the auspices of the Abbott Medical Student Fellowship in Nuclear Medicine. One resident in pathology was here for six months as part of the combined program with St. Mary's Hospital in Knoxville. Three one-year trainees from this country and two physicians from foreign countries were also here for one-year fellowships.

The program for these groups varied, depending on the particular training mission, but were built around the clinical program with participation in formal ward rounds, in the study and treatment of patients, in evaluating diagnostic radioisotope tests and the management of patients containing radioisotopes; in addition they were oriented to the major current clinical program on the total-body irradiation studies, marrow-graft attempts, and the study of the effects of radiation. Each of these trainees was also scheduled for the ORINS Special Training Division's basic course in radioisotope techniques in addition to the shorter instructional seminars of the Medical Division. Training aids are available for manipulation and study, and residents participated in the various conferences. In addition to the three half days per week of formal ward-round sessions, a weekly seminar in hematology was presented on Tuesday afternoons. A Friday noon work conference was also initiated to which residents were invited. Physicians here for longer than four months are expected to participate in one of the research projects of the division. As before, this has proved to be valuable to the program and has given the trainee experience in clinical basic investigative work.

Research Participant Program

This continuing program has been a distinct asset to the goals of the Medical Division. During the summer of 1960 there were five visitors representing medical school or undergraduate faculties in biochemistry, pharmacology, microbiology, and chemistry. From each one, a productive piece of work resulted. The participants added the skills of their own disciplines to the Medical Division program and in return received training both in details of the research project and special help in radioisotope methodology — for example, chromatography or liquid beta scintillation counting.

In support of this research-participant program, two college students and one graduate student also joined the program, two of them under the University Relations Division's Student Trainee Program. These "apprenticeship" relationships were highly successful in providing the additional man power for the experiments undertaken and also gave to these students a worthwhile experience in a research setting.

Qualification Courses and Special Seminars

The qualification courses, given in separate one-week sessions as Preclinical I, Preclinical II, and Pathology, were continued. Some changes in the approach to certain topics and experiments have been necessary, but major alterations have not been required. As before, Preclinical I introduces language and tools, principal topics presented in half-day or one-day sessions. Preclinical II introduces application of the principles presented in Preclinical I using the same approaches to acquaint the students with instrumentation and measurement, and concepts they use in clinical methods. The third week is devoted to clinical diagnostic procedures that are performed by the students to meet AEC license requirements.

The special short course for 1960 was in autoradiography, was limited to eight participants and three auditors, and was a fairly intensive and detailed course emphasizing laboratory participation.

Miscellaneous Training Activities

Revision has been started of the 37 midget exhibits presenting minimum basic data that a physician must know to use radioisotopes. In addition, plans for an open-ended series of exhibits on applied techniques are under way and some of these have been prepared. Selected groups of these midget exhibits have been presented at national meetings.

Members of the staff presented a symposium entitled "Training Aids" to the spring meeting of the Southeastern Chapter of the Society of Nuclear Medicine. They also were invited to present the annual evening symposium at the 1960 annual meeting of the Society of Nuclear Medicine. The topic was "Tools of the Trade." To a very large audience, the staff demonstrated and described the devices proven successful in the ORINS training of physicians in radioisotopes.

Requests for thyroid uptake manikins continued to be received and these kits have been shipped to widely divergent geographical locations — Atlanta, Georgia; Decatur, Illinois; Los Angeles, California; Boston, Massachusetts; Sydney, Australia; Bonn, Germany.

APPENDIX III

Medical Division

PUBLICATIONS FROM THE MEDICAL DIVISION (FISCAL YEAR 1961)

Andrews, G. A. "Medical Students and Radioisotopes." The New Physician 9, No. 12, 23-27, 1960.

and Adipose Lipids During Cerium-Induced Fatty Liver Infiltration." Fed. Proc. 20, 275f, 1961.

Tsuya, A. and Hayakawa, I. "Linear Scanner (ORINS): Possibility of its Clinical Application." Acta Radiologica Japonica 20, 2001-2013, 1960 (in Japanese).

PATIENT DAYS

July	493
August	487
September	439
October	501
November	517
December	472
January	493
February	384
March	496
April	372
May	386
June	312
Total Patient Days	5352
Average Per Month	446
Average Per Day	14.6

ISOTOPES USED BY MEDICAL DIVISION

Arsenic 74	11.	mc
Calcium 47	1	mc
Carbon 14		
Formic Acid	1.20	mc
Chlorine 36	.050	mc
Chromium 51	8.0265	mc
Cobalt 57	0.30245	mc
Cobalt 60	1.48545	mc
Gold 198	970	mc
Iodine 131		
Oriodide	6346	mc
Risa	22.5	mc
Radiocaps	37.94	mc
Rose Bengal	8.75	mc
Uracil	0.3	mc
Iodine 132	10.0	mc
Iron 59	.75	mc
Iron 59 (P)	250.6	mc
Lanthanum 140(P)	190	mc
Lutecium	149	mc
Mercury 203	8.1	mc
Phosphorous 32	284	mc
Potassium 42	2	mc
Rachromate	4	mc
Raolein	.77	mc
Rubidium 86	1	mc
Sodium 22	.60	mc
Sodium 24	1	mc
Sulfur 35 (P-1)	121.5	mc
Trithyrotope Solution	.5	mc
Triomet	4.2	mc
Yttrium	283	mc

MEDICAL DIVISION CLINICAL CONFERENCES — 1960

July 7: Certain analytical problems and proposed methods—G. C. Kyker.
July 14: Treatment of hypersplenism by irradiation of the spleen—F. Comas.
July 21: Porphyrins—Ray Hayes.
July 28: Thyroid physiology in diagnosis—Staff.
August 4: Current problems in thyroid carcinoma localized to neck—Staff.
August 11: Changes in liver of irradiated, bone marrow treated mice—Arthur L. Kretchmar.
August 18: Audiotaped E. O. Lawrence Memorial Lecture—by Edward Teller, as presented at the 1960 Society of Nuclear Medicine meeting.
August 25: Fe-59 in clinical hematology—W. N. Tauxe.
September 1: Report on conference on chemical organization of cells—Helen Vodopick Goswitz.
Septembr 8: Bone marrow transplantation in primates and secondary disease in primates and man—Lodewijk Marius van Putten.
September 15: The acute radiation syndrome in the rabbit—Herbert B. Gerstner.
September 22: Therapeutic use of I-131—B. W. Sitterson.
September 29: Some problems in the DNFB determination of taurine—Ben Dowdey.
October 6: Multiple myeloma—David White.
October 13: Poorly differentiated malignancy presenting as enlargement of axillary lymph node—Bill Nelson.
October 20: Effect of cerium on fatty acid mobilization — Fred Snyder.
October 27: Radioisotopes in medicine, decay made easy, the Rehovoth conference—Marshall Brucer and D. A. Ross.
November 3: Trilinear chart of the nuclides—Marshall Brucer and D. A. Ross.
I-131 treatment of thyroid cancer in pregnancy (case report)—Herbert Gerstner.
November 10: Instrumental pH colorimetry—G. C. Kyker.
November 17: Oxidative phosphorylation—Robert C. Nordlie.
December 1: Midget Exhibit No. 4—Properties of radiation — Marshall Brucer; Penetration of radiation—Ray Hayes; Clinical-pathological conference—Robert Johnson and Ralph Kniseley.
December 8: Midget Exhibit No. 5—Interaction of gamma rays—Marshall Brucer; Interaction of gamma rays—D. A. Ross.
December 15: Thyroid physiology in diagnosis—Arthur L. Kretchmar.
December 22: Midget Exhibit No. 6 — Interaction of charged particles—Marshall Brucer; Detection of charged particles—D. A. Ross.
December 29: Resin uptake of I-131—triiodothyronine from serum; ranges of values for patients with thyroid disease and other conditions—Ray Villalva.

MEDICAL DIVISION CLINICAL CONFERENCES — 1961

January 5: Midget Exhibit No. 7—Nuclear Physics Devices—Marshall Brucer; Cyclotron production techniques—Ray Hayes.
January 12: Spleen and liver weight correlation in mice with bone marrow grafts—Arthur L. Kretchmar.
January 19: Midget Exhibit No. 8—The levels of radiation— Marshall Brucer and Roger Cloutier.
January 26: I-131 therapy of thyrotoxicosis and carcinoma of thyroid—Staff.
February 2: Midget Exhibit No. 9—Radiation safety — Marshall Brucer and Roger Cloutier.
February 9: Two cases of anemia of undetermined etiology—Helen Vodopick Goswitz and Frank Goswitz.
February 16: Midget Exhibit No. 11—Protection devices—Marshall Brucer and Roger Cloutier.
February 23: Idaho Falls reactor accident: preliminary pathologic report—C. C. Lushbaugh.
March 2: Effect of total body irradiation on fatty acids of plasma and central nervous system—Fred Snyder.
March 9: Sickle cell anemia with positive coombs and LE cell preparation—Frank Goswitz.
March 16: Midget Exhibit No. 14—Instructions in case of accident—Marshall Brucer and Gould Andrews.
March 23: Midget Exhibit No. 12—Contamination; Midget Exhibit No. 13—Waste disposal—Marshall Brucer and Roger Cloutier.
March 30: Therapeutic uses of I-131—Staff.
April 6: Rapid reprocessing of scan records—P. R. Bell, J. E. Francis and C. C. Harris.
April 13: Thrombotic thrombocytopenic purpura—Helen Vodopick and Bill Nelson.
April 27: I-131 in diagnosis of thyroid disease—Staff.
May 4: Case presentation—Hodgkin's disease treated by total body irradiation—Helen Vodopick Goswitz.
May 11: Midget Exhibit No. 19—Instrument for radiation detection; Midget Exhibit No. 20—Instrument for radiation measurement—Marshall Brucer.
May 18: Some general thoughts on the treatment of cancer—Gould Andrews.
May 25: Diagnostic procedures for thyroid function—Arthur L. Kretchmar.
June 1: Midget Exhibit No. 15—Mathematical tools — Marshall Brucer and G. C. Kyker.
June 8: Midget Exhibit No. 16—Characteristics of measurement—Marshall Brucer and Craig Harris.
June 15: Studies on tissue oxygen levels—F. Comas.
June 22: The effects of local irradiation (Co-60 teletherapy) on peripheral blood and bone marrow—Frank Goswitz.
June 29: Midget Exhibit No. 17—Counting statistics—D. A. Ross and Marshall Brucer.

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Oak Ridge Institute of Nuclear Studies

Sixteenth Annual Report

OPERATING UNDER CONTRACT

WITH THE

United States Atomic Energy Commission

JUNE 30, 1962

Medical Division

The Division increased its emphasis on the study of radiation effects. Patients have been given total-body irradiation in order to assess clinical, hematological, biochemical, and immunological responses. These results have been pursued simultaneously with studies in experimental animals emphasizing particular aspects of radiation effects, especially the biochemistry of homologus disease and the effects of radiation on the fat of the bone marrow.

During the year much attention was given to the design and construction of a total-body counter that will greatly augment the effectiveness of the Division's program in studying metabolism and distribution of certain important radioelements.

RADIATION EFFECTS AND TREATMENT

Additional recent experience has given further evidence that total-body irradiation in a dose of about 300 r (without bone marrow treatment) can produce remissions in some patients with acute leukemia. In these patients, hematologic recovery begins earlier than in normal persons accidentally irradiated at about the same dose; the significance of this is not known. This earlier recovery after therapeutic irradiation also has been reported in some of the patients irradiated in other clinics for kidney transplants. Further work is being done to clarify these time patterns of hematologic effects of large doses of radiation.

Total-Body Irradiation at Relatively Low Doses

Since September 1959, twenty-seven patients with chronic leukemia or malignant lymphoma have received total-body irradiation in doses of 50 or 100 r. This treatment has been used for many years in various hospitals but is usually given in divided doses. It was decided to give a single dose, so that the time of the response could be clearly related to the time of the dose. Most patients had no early symptoms attributable to radiation therapy, but an occasional patient complained of nausea or lack of appetite, or both, on the day of therapy or the following day. With two exceptions, these symptoms were limited to the 100 r group.

In patients with chronic lymphocytic leukemia, doses of 50 or 100 r produced a gradual diminution in lymphocytic count, and enlarged lymph nodes usually shrank somewhat. Most of the patients had subjective improvement. In the smaller group of patients with chronic granulocytic leukemia, distinct hematologic responses were always seen and some clinical improvement was usual. No significant benefit was noted at these dose ranges in three patients with Hodgkin's disease.

Perhaps the most significant results have been obtained in lymphosarcoma. Here regression of enlarged lymph nodes was greater than expected and in one patient a rather remarkable improvement in the bone marrow took place, with disappearance of extensive lymphoid infiltration.

Bone Marrow Lipids in Animals Given Total-body Irradiation

The amount of fat of the bone marrow increases after total-body irradiation and a study on this has been undertaken in animals. Specific questions under investigation are: (1) the quantity of increased lipid in irradiated marrow; (2) the chemical composition of the fat as compared with the normal marrow fat and with other body fat stores; and (3) physiological implications of these qualitative and quantitative changes in relation to the metabolism of marrow cells or the metabolism of the whole animal. Studies in rats have shown that the increase in marrow fat following irradiation is largely due to an increase in triglycerides.

Studies of Homologous Disease

Homologous disease, which has also been called foreign bone marrow disease and secondary disease, occurs in experimental animals after they have been given lethal or near lethal doses of radiation and donations of blood-forming tissues from healthy donors that are not identical in strain. The animals that receive the donor tissue survive the ordinary period of radiation death but develop a later disease characterized by weight loss (in spite of a good appetite), failure of hair growth, and disorders involving the lymphatic tissue. It is believed that this disease is caused by an immunologic reaction between the host and donor tissues. Evidence indicates that in most situations the major factor is the reaction of the donor tissue against the host. This problem has great potential importance since it seems to be a major limitation in the treatment of high-dose radiation injury with bone marrow grafts, and also may be a major limitation in the therapeutic use of other types of tissue grafts in humans.

Cooperative studies at the Institute and the Oak Ridge National Laboratory have indicated that enlargement of the liver is a major feature of secondary disease. Further evidence has recently been derived from biochemical data on the livers of these animals. Nitrogen content is temporarily reduced by radiation, and fat content is not much affected. These findings tend to rule out a degenerative process as an explanation for the enlarged liver, and suggest an increase in cytoplasm, for this is the major cellular location of nitrogen and phosphorus. The microscopic study of the livers of these animals also indicates that the enlargement is mainly in the cytoplasm of the cells.

The aspartic acid of the livers of these animals increases above normal, beginning about the third day after irradiation and bone marrow administration. It remains elevated for at least 35 days, with maximal levels reached on the seventh day. It is believed that the graft disrupts the balance of formation and utilization of aspartic acid in the liver. The increase may be the indirect result of increased production of purines and pyrimidines, which causes the formation of excess glutamate. The glutamate, in the presence of the liver transaminase system, yields aspartic acid. This complex biochemical evidence may indicate that the animals with secondary disease are undergoing a period of very great activity of antibody-forming cells, and that the demand for purine and pyrimidine from the liver is for the formation of nucleic acid in these cells. Additional tracer studies are under way to try to clarify this effect. Possibly, the changes in the liver in secondary disease are similar to those in the general debilitating process occurring in patients with extensive cancer—so-called cancer cachexia. If so, these studies will have even broader significance.

Teletherapy

The teletherapy program was started ten years ago with the main intent of developing and perfecting machines for external irradiation, using radioisotopes as the source of radiation. Cobalt-60 and cesium-137 were found to be of value and many of the present machines now in use throughout the world were influenced by these early ORINS efforts. At present, the teletherapy program no longer concerns itself with design of new machines, but rather with their clinical application in the treatment of disease. The program is restricted to limited numbers of special groups of patients. Some of these are chosen for evaluation of radiotherapeutic possibilities (hypersplenism, carcinoma of the bladder). Some are patients admitted to the Division for other studies who also require radiotherapy. Opportunities for related studies are sometimes afforded, for example, the work on effects of local irradiation on bone marrow.

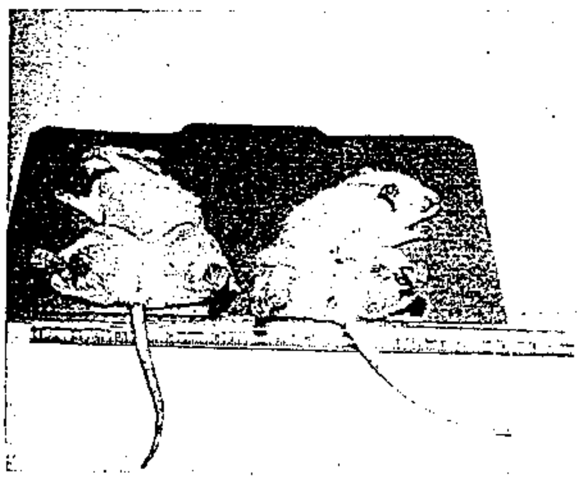
Many patients treated have leukemias and lymphomas; this is because of the research interest of the Division in this group of conditions. The problem of detecting occult retroperitoneal lesions in patients known to have lymphoma has been solved in some patients by performing laparotomies after which ports for radiation therapy are planned.

A consecutive series of patients having carcinoma of the bladder with invasion of the bladder wall is part of a study of epithelial tumors. The purpose is to try to determine some of the reasons for the poor results obtained in the treatment of this disease. In the past, failure may have been due to the difficulty in assessing the true extension of the tumor and pelvic metastases by the usual means of tumor localization (clinical examination, radiography, and cystoscopy). In this series each patient had an exploratory laparotomy for the purpose of mapping out the tumor and searching for lymph node metastases. As soon as the patient recovers from the operation, treatment with cobalt-60 teletherapy is begun. Twelve patients have been treated so far: six have already died (one of unrelated causes and with no recurrence); five patients are living but with persistent disease; and one patient is alive with no evidence of recurrence. Although the series is still small, it is clear that extra effort to determine accurately the extent and location of the tumor will not result in a higher percentage of cures. This interpretation is strengthened by the fact that in the failures, tumor persistence or recurrence was always at the primary site.

Influence of Oxygen Tension on Related Radiosensitivity of Tumors

Tumors are more sensitive to radiation when they have a large supply of oxygen and are more resistant to radiation when they are deficient in oxygen. An attempt has been made in England to use this phenomenon clinically by having patients breathe in an atmosphere of increased oxygen tension while they are receiving local radiation to tumors. The theory is that the tumor will be made more sensitive to radiation while the sensitivity of normal tissues will not be greatly changed. However, problems have been experienced. To achieve increased oxygen saturation in the body is difficult, particularly in tumors, for they often have a poor blood supply. For this reason the increase in tumor radiosensitivity may be slight.

An investigation has been undertaken to study the opposite technique—reducing the oxygen tension in the body during radiation therapy. Since the tissues immediately surrounding the tumor may have a better blood supply than the tumor, this reduced oxygen tension will be more pronounced in the tissues around the tumor, and a relative increase in the radiosensitivity of the tumor may be gained. On this basis larger and more effective doses to tumors might be given without increasing the damaging effect in surrounding tissues. Preliminary studies on rats have been made to try to demonstrate whether this can be achieved. Tumors are implanted in the thigh and oxygen is reduced by temporarily occluding the large artery going to the leg on the side of the tumor. Bone marrow is studied as an example of a normal tissue in the same region. The special device used for measuring the oxygen tension consists of small platinum needles that are inserted into tissues to record an electrical current proportional to the oxygen level. Tritiated thymidine is used to indicate the degree of desoxyribonucleic acid synthesis in the tumor and in the bone marrow after radiation in the presence of anoxia. Results so far show that occlusion of the blood vessel has a definite protective effect on the normal bone marrow.



Study of the effect of oxygen on irradiation of tumors. These rats had tumors implanted in both legs on the same day. The animal on the left received no irradiation. The animal on the right was irradiated while the blood supply to the left leg was cut off. The tumor on the right leg is smaller, indicating that irradiation is more effective when the tumor is oxygenated. Similar changes occur in the bone marrow of the leg. The scar on the abdomen of the rat on the right is a result of an operation performed seven days earlier when the artery to the left leg was clamped and irradiation was given.

Effects of Local Irradiation (Cobalt-60 Teletherapy) on the Peripheral Blood and Bone Marrow

While there have been many published studies concerning the effects of total-body irradiation on peripheral blood and bone marrow, there are few reports dealing with the changes produced by local port irradiation. Further work was done on this problem during the year. Eight patients, six with carcinoma of the urinary bladder and two with carcinoma of the lung, were treated with cobalt-60 teletherapy, in general a four- to five-week course totaling about 6000 r. Bone marrow was aspirated from the irradiated sites before therapy, at midtherapy, at the completion of therapy, and at one, two, three, and four months postirradiation. Marrow was aspirated from control sites, not in the field of irradiation, at most of these times. Local irradiation was followed by a reduced total leukocyte and absolute lymphocyte counts in the peripheral blood. The bone marrow demonstrated no morphologic changes in control sites after port irradiation. The marrow in the irradiated sites showed a profound loss of cells and did not regenerate during the four months after therapy. However, in some of these heavily damaged marrows there was persistent incorporation of tritium-labeled thymidine into the remaining blood cell precursors, suggesting that some potentiality for recovery exists and that the failure of cell repopulation may be due to something other than a lack of precursors.

RADIATION PHYSICS AND INSTRUMENTS

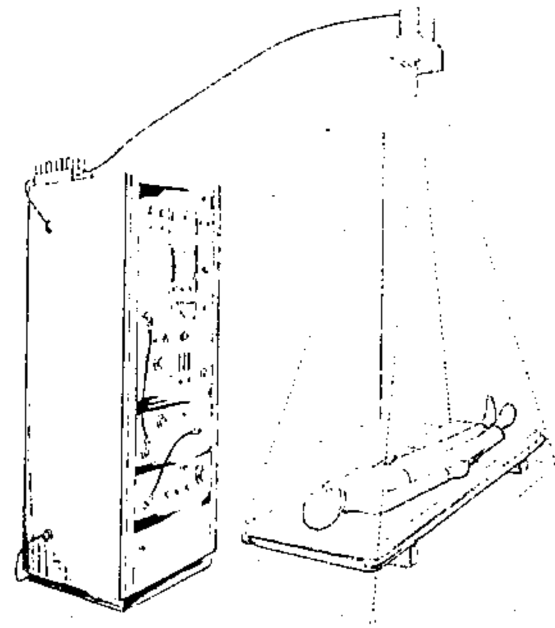
Whole-patient Counting

The value of measuring the total radioactive content of a patient or a normal person has been amply demonstrated. The procedure is useful in rate-of-turnover and other physiological studies; in toxicological investigations; in clinical diagnosis; in the back-calculation of accidental neutron dosage; in monitoring the intrusion of fallout—via air, food, and drink—into "normal" people; and in evaluating the therapeutic problems arising from a wide variety of contaminating accidents.

Many patients who come to the ORINS hospital could be studied advantageously by this method, and plans and designs have been under way for the past three years. Difficult problems arise when an attempt is made to count the activity in any large-volume sample at near background levels.

These problems center mainly around the nature and arrangement of the detector and its shielding enclosure, but also include the analysis, recording, and storage of data. A serious problem exists in the ORINS operation: the huge range of activities the patients present. They may contain anywhere from one or two hundred millicuries (of iodine-131, for example) down to a few hundredths of a microcurie, where the levels merge into the body backgrounds found in normal people. No single instrument covers this large 50 million-to 1 range. Such an instrument could be designed, but it would be very costly. Accordingly, the plan is to have three whole-patient counters: one for the high-dose range ("hot-patient counter"), one for the intermediate range ("warm-patient counter"), and a costly "cool-patient counter" for tracer-dose patients and normal people, whose count rates will be very little above surrounding background.

Hot-patient Counter. A counter of this type is already in use. Since high sensitivity is unnecessary, the detector-to-patient distance can be made large—about 2½ meters—resulting in more nearly uniform and easily repeatable positioning of the detector. The patient lies supine on a stretcher a little above the floor; a basement floor is used so that there is no significant radioactivity beneath him. If distribution is uneven he can be counted both supine and prone, and the results can be averaged. The detector is a 2-inch by 2-inch cylindrical, sodium iodide crystal looking down from up near the ceiling. Moderate lateral shielding, of



"Hot-patient Counter," range: 100 millicuries → 25 microcuries.

lead, is used to keep the background down to a reasonable level. With the bare crystal, iodine-131 can be counted in quantities down to about 25 microcuries, but since a patient with 100 millicuries would overload even this distant detector and its supporting circuitry, two lower stages of sensitivity have been made possible by means of removable slabs of ½-inch lead, each of which reduces the radiation reaching the crystal by a factor of 10. In this way a working range of around 4,000 to 1 has been achieved.

Data bearing on the usefulness of this counter are accumulating and improvements are being made in the method of operation. Since a "monocular" detector, viewing the patient from one side only, is likely to be compromised by the absorption of some radiation within the source, it becomes highly desirable to use a realistic phantom in counting the dose (or a known fraction of it) for comparison with the patient. But patients vary widely in dimensions if not in composition, and an artificial phantom is hard to devise. The feasibility of using the patient for the phantom is being studied by counting him as soon after administration of the dose as it becomes evenly distributed and before it becomes concentrated in the stomach, bladder, or thyroid gland.

Most of the data collected so far deal with the movement of iodine through the patient: (1) when some normal thyroid tissue is present; (2) when nctioning thyroid cancer is present, but no normal tissue; and (3) when no thyroid tissue, either normal or malignant, is there. The most rapid disappearance occurs, of course, when no thyroid tissue is present to capture the administered iodine; in a patient who has had a total thyroidectomy for cancer of the thyroid one should promptly suspect the presence of hidden metastases if this disappearance does not occur. This series of patients is still small, but it is being expanded as suitable patients are referred to us.

Warm-patient counter. Design of a permanent warm-patient counter has been postponed until more is learned from the low-level and high-level counters. Meanwhile, the use of the present linear scanner for intermediate activity levels is being explored. The linear scanner's normal job is to sweep the patient through a detecting gap to plot a contour of count rate in terms of position along the long axis of the body. This tells us in what cross-section of the patient the administered activity is concentrated. But a scaler can be put on the detectors and add up the pulses as the sweeping process goes on, and the total gives a measure of whole-body count.

Cool-patient Counter. This is the whole-body counter in the usual sense, designed to provide a high-sensitivity detector located in a special counting room where great pains are taken to reduce surrounding background to an extremely low level. To provide a suitable location for this counter, an underground extension from the north end of the middle floor of the hospital is being built. The patient about to be counted will leave his clothing in an undressing room, take a shower to wash off any surface contamination, and put on a clean nightgown. He will lie on a stretcher supported on a track system so that he can be pushed through a circular opening into a steel-and-concrete-shielded counting room. Analyzing, processing, and recording equipment will be located in the adjoining clean laboratory. The detectors will provide for spectral analysis so that the various radionuclides present even in normal people can be sorted. This new facility is scheduled for completion in late 1962.

Total-body Irradiation Dosimetry

Aqueous chemical dosimetry is a convenient method for the measurement of absorbed dose, for such dosimetry systems can be placed in suitable containers to act as phantom media. The ferrous sulfate system has been used to determine the effect of body size on absorbed dose in the ORINS cesium-137 total-body irradiation facility. Compartmentalized phantoms simulating an adult, an adolescent (12-year-old), and a child (3-year-old) have been used. The compartmentalization made possible the determination of the average absorbed dose to the different parts of the anatomy as well as the average dose to the total body. The ratios of the adolescent and child average total-body absorbed dose to that for the adult were 1.05 and 1.07 respectively. Similar ratios for the various phantom compartments did not exceed 1.12. In previous depth-dose measurements in these same phantoms, the lowest percentage of the air dose encountered was 46%, 52%, and 65% respectively for the adult, adolescent, and child. These measurements indicate that the design of the total-body irradiation facility effectively overcomes dose variations due to differences in body size.

ORINS-ORNL Scanner Evaluation Program

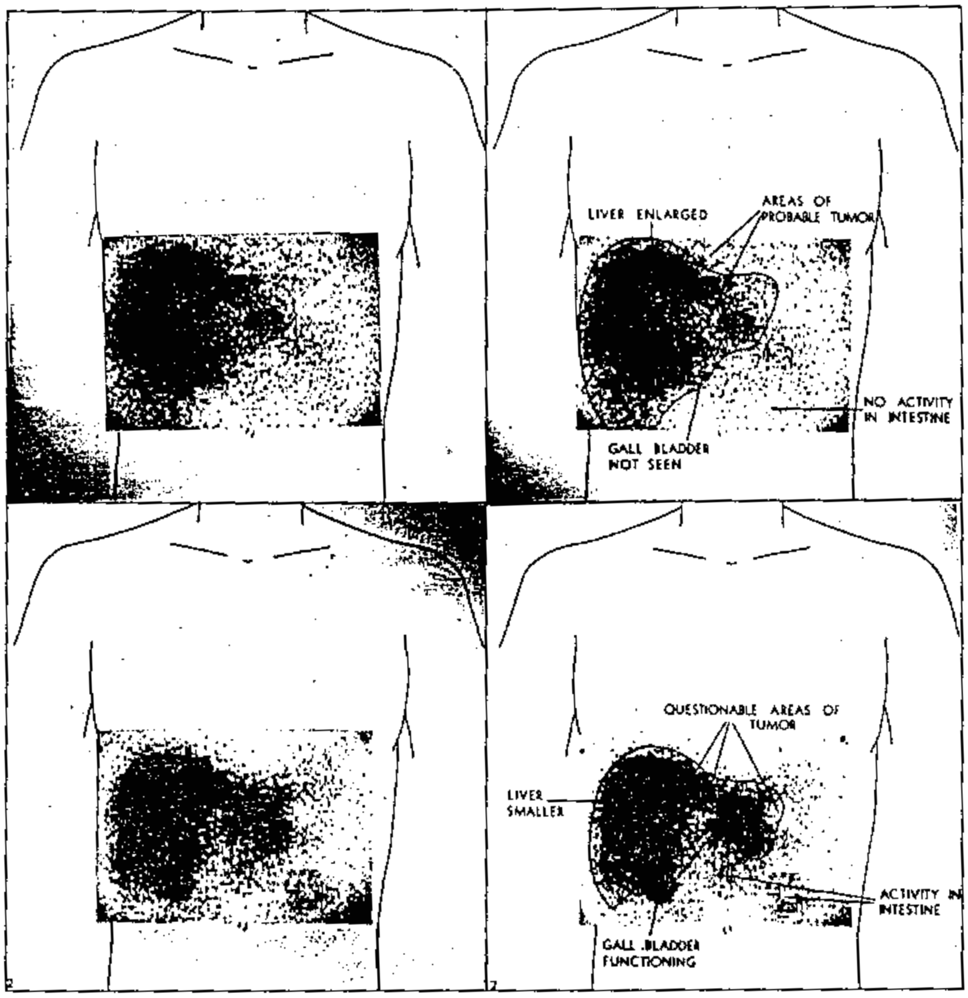
In November 1959, the prototype of a new radioisotope scanner developed by the Medical Nuclear Instrumentation group at the Oak Ridge National Laboratory was placed in clinical service at the Division. Evaluation of the scanner in clinical service was started to test the success of improvements in collimation, electronics, and recording embodied in the scanner. An outstanding improvement offered by this scanner is a 37-hole, honeycomb collimator fabricated in gold, with surrounding lateral shielding of tungsten. The gold provides greatly increased opacity between the focusing holes, while the tungsten gives enhanced suppression of the patient's body background. These features are of special value during the scanning of intracranial tumors, where the target to nontarget ratio often is low.

The scanner was first used in studies on thyroid disease, and in localization of metastatic thyroid carcinoma. To broaden the clinical use, a program of localization of intracranial neoplasms was started in cooperation with regional neurosurgeons. In addition, liver scanning studies are being done.

The scanner has operated more than 22,000 hours, with less than 50 hours for maintenance and repairs. Several important modifications to the control system were made, and the scanner use is now simpler and operator errors are less likely. The digital photorecording system has been improved and shows promise of improving the clinical interpretation of scan records.

Brain Scanning. Several tracer compounds have been used, with radioiodinated human serum albumin serving as a "standard." Arsenic-74 (sodium radioarsenate) and Hg^{203}-Neohydrin were used. Positive evidence of space-occupying lesions was found in 17 of 40 patients. Confirmation at surgery or autopsy was obtained in 10. Two were considered confirmed only by conventional radiographic techniques. No confirmation has been obtained in 4 patients; neither has significant disease been ruled out. The remaining positive scan was a doubtful localization; surgery showed a diffuse hemorrhagic condition in the region of the indicated "lesion." No other false positives were obtained. One subdural hematoma, known to exist, was not visualized. Some of the negative scans, particularly of the "doubtful-negative" class, may yet be shown to be on patients with lesions that were missed. In those confirmed surgically, the scan record appearance of the tumors agreed with actual tumor outlines.

Several of the brain scans have been used as



Two pairs of scans on a patient with cancer involving the liver. All scans were prepared after an intravenous dose of rose bengal labeled with iodine-131. The two upper pictures are of the same scan: the one on the right has had additional marking to help with interpretation. It shows the findings during a period of obstructive jaundice caused by metastatic cancer. On the basis of this scan, the patient was given external therapy with cobalt-60 to the areas of apparent tumors in the mid-part of the liver. Subsequently the jaundice cleared, the patient improved, and the second scan was obtained (lower half of the composite). Again, the scan at the right is a copy of the one at the left and has had additional markings to help with interpretation.

test cases in the development of a data-extraction method, in which a scan record is scanned to produce a more easily interpretable record.

Liver Scanning. For the study of liver disease, mainly colloidal gold-198 and iodine-131-labeled rose bengal (both administered intravenously) have been used. A few scans using iodinated human serum albumin have been run in patients with metastatic liver disease, but these have not been rewarding. Rose bengal is much more informative. The patient is first given 150 to 300 mg of stable rose bengal and (about 10 minutes later) 0.3 to 0.5 millicurie of the iodine-131 preparation. Displacements of the liver from the normal position, changes in size or shape, and the presence of any reasonably large tumor or cyst are usually well shown. In a few cases of lymphoma the patchiness of the liver scan suggested irregular liver involvement. Abnormalities of gallbladder and biliary tract function may be shown; emptying of the gallbladder into the intestine is signaled by the appearance of dark patches in the upper-intestinal region. Rose bengal does not provide a spleen shadow; gold-198 does so, although only weakly.

Thyroid Scanning. In thyroid disease the scans have been particularly valuable, especially in thyroid carcinoma. Scans are helpful in the estimation of thyroid volume in hyperthyroidism, particularly after partial thyroidectomy. On the other hand, nodules are often difficult to see (as shown by subsequent surgery) unless they are of the hyperfunctioning type. Moreover, it is difficult to tell a hypofunctioning nodule from a nonfunctioning one with overlying thyroid tissue, and small nodules may be missed entirely.

The Oak Ridge National Laboratory scanner's improved suppression of nontarget activity now shows physiological structures that were formerly masked. This often happens in patients with total thyroidectomy, where the dose of iodine-131 is large and the relatively high body background formerly penetrated the sides of the leaky collimator. In an uninvolved chest, the normal, slight darkening of the heart and mediastinum can now be seen as compared with the "clear" lung fields on either side. Sometimes, in an athyroid neck, a faint, vertical streak of activity can be noted lying a little to the left of the midline and extending an inch or so above and below the jugular notch of the sternum. This might represent iodine held in the mucous secretions of the esophagus or trachea. Again, with the new scanner, oral iodine is almost routinely seen, perhaps caught in the tartar on the teeth; salivary glands are often seen and sometimes the nasal or lachrymal glands or both will darken the area of the nose.

In the abdomen the stomach shadow is regularly observed as heretofore, but now a weak shadow may be seen contributed by the airless and metabolically active liver, which will sometimes outline the right leaf of the diaphragm. Vague blobs of darkening are found throughout the abdomen; these are usually due to intraintestinal iodine, but this is not certain until they move, either spontaneously or in response to manual manipulation or to a cathartic or an enema. In one cancer patient an area of this kind refused to budge, and it was ultimately traced to a bony metastasis in the ilium. Radioiodine in the intestinal tract is a severe problem in a linear scan, for it may simulate a functioning area of tumor.

The general result of the improved scanning equipment is that while weak thyroid metastases and brain tumors can be seen better than before, a number of normal shadows that call for considerable care in interpretation also are seen. The instrumental improvement has required a readjustment of standards.

Collimation of *in vivo* Studies of Distribution of Chromium-51 and Iron-59 in Spleen and other Organs. The value of in vivo studies of the distribution of chromium-51 and iron-59 has been increased by the investigation of the physical factors influencing external counts over organs such as the spleen, with primary attention to the effect of collimation. Isoresponse curves were plotted for a commercial collimator applied to the side of a large plastic tank filled with water. A small chromium-51 source was placed at multiple locations in the water and counts were recorded for each location. This was repeated with an iron-59 source. Similar curves were plotted for the same detector without the collimator, so that the crystal could be applied directly to the water tank. Subsequently, spleen and liver phantoms containing chromium-51 and iron-59 solutions were counted in the water tank. The data show that shorter collimators not only increase the sensitivity of external counting over an organ near the surface but reduce the error due to faulty positioning and minimize body background.

MEDICAL NUCLIDES AND LIPID METABOLISM

Radiation Dose to the Gastrointestinal Tract of Human Beings

Unconfined radioactive materials constitute both a potential internal and external radiation hazard. The possible internal dose may well be more serious. Dangerous amounts of radioactivity may be accidentally carried directly into the intestinal tract through the oral ingestion of contaminated food and water, or indirectly through inhalation and subsequent swallowing. If the ingested radionuclides are not absorbed into the blood stream, their radiation dose will be delivered mainly to the intestinal tract. A large fraction of the radioactivity produced by reactors and nuclear explosions is of this type.

Recommendations on the maximum permissible concentrations for various nuclides in air and water are based on a "standard man" model of average human behavior where the intestinal tract is the critical organ. It is recognized that people may vary considerably with respect to the actual dose received from a particular level of contamination. The extent of the variation for the dose received by the lower large intestine in patients is the subject of a current study at the Division. Extensive variations found in previous in vivo dose measurements in animals prompted this investigation. The technique involves giving a safe tracer dose of lanthanum-140 by mouth and recording the fecal excretion in terms of percentage of dose excreted and time of passage through the gastrointestinal tract. From these data and from the known information about the rate of passage through the stomach and small intestine, the dose to the large intestine, where it stays longest, can be calculated. The methods are applicable to beta-emitting isotopes of any half life. The data obtained indicate a great variation in humans. In an extreme example, one patient received 35 times the dose to the intestinal wall that another received from the same amount of ingested isotope. In general, the results confirm that accepted maximum permissible dose levels for ingestion of poorly absorbed radioisotopes of long half-life are approximately correct. The results, when extrapolated to radioisotopes of short half-life, suggest that these may be less hazardous than currently believed and that the maximum permissible levels could be safely made somewhat higher.

Studies of Fat in the Bone Marrow of Irradiated Animals

Perhaps the most striking and important effect of total-body irradiation is the reduction in the number of blood-forming cells in the bone marrow. Along with this reduction there is an increase in fat in the marrow. Studies done with silicic acid microcolumns, thin layer chromatography, and gas liquid chromatography have brought forth new information on the nature of the fat change in the marrow of rats after total-body irradiation. The fat increases up to about 4 or 5 times the normal level. The increase in fat is mainly made up of triglycerides but other fatty fractions are present, including a distinctly abnormal amount of phospholipids. Fat in the marrow before and after irradiation is chemically much like that of the adipose tissue in liver. It is not known, however, whether the increased marrow fat following radiation results from mobilization of fat from other parts of the body or from new formation of fat in the bone marrow. In the past, little attention has been given to the considerable amount of fat found in normal bone marrow, but it may not be an inert material, and evidence is developing that the fat content of any tissue is important in its total metabolic activity. Further studies will help to clarify the source of the increased fat in the marrow after irradiation.

The Effect of Stable Cerium on Fat Metabolism

Development of a striking fatty liver in rats after stable cerium is administered intravenously has been under study for several years. Cerium is an example of a group of elements, similar in chemical behavior, that are important because they occur in fission products; several of them cause the fatty liver change. Earlier reports indicated that development of the fatty liver was related to hormonal factors and that a fall in blood sugar levels was an important feature of the cerium effect. Correction of the blood sugar levels by extraneous methods would tend to prevent the development of the fatty liver. Removal of certain endrocrine glands would also prevent the development of the fatty liver.

Additional work on this problem during the year centered around the chemical composition of fats that accumulate in the liver, and the ability of the liver to release fat for use in other tissues. The The use of thin-layer chromatography has revealed that the fatty acid composition of triglycerides rom adipose and liver tissues is identical in both untreated and cerium-treated rats. The increase in the liver fat following cerium is made up of triglycerides and the total fatty acid composition of the liver lipids under these conditions thus becomes similar to that of adipose fat. The fact that triglycerides are not qualitatively affected by cerium indicates that the esterification of fatty acids in the liver is not selectively altered by cerium. The use of carbon-14-labeled fatty acids to assess the relative turnover of the fatty acid occurring in triglycerides is expected to yield additional evidence on the previously presented concept that an increased mobilization rate of adipose fat to the liver is the main feature in the cerium-treated rats. Although cerium alters certain enzyme systems, this has not been demonstrated as a triggering mechanism for the fatty infiltration. A special procedure involving the use of Triton, a surface-active agent that prevents the escape of triglycerides from the plasma, has shown that a lowered release of glyceride from the liver is not an important factor in accounting for the fatty liver induced by rare earths.

Intralymphatic Injection of Internal Emitters

Solutions of yttrium chloride and cerium chloride were observed to localize selectively after intralymphatic administration in dogs. These results suggest an approach to the selective irradiation of lymph nodes in the drainage of a specific organ or surgical field. The similar behavior of yttrium and cerium indicates that the lanthanons as a group are available for this type of use and these radioisotopes offer a wide choice in radiation characteristics.

Radioactive preparations were injected into a lymphatic made visible in the hind foot of a dog by a previous interstitial injection of indirect Sky Blue. Radioassay emphasized measurements in blood, liver, spleen and lymph nodes both in the path of drainage and from the opposite side.

The fraction in the popliteal and iliac nodes on the injected side exceeded that in liver and spleen, sometimes several fold, with a relative radioactivity usually several hundred times that of the next most concentrated localization. The volume of the dose and its rate of injection appear to be important factors, as do the nature and dose of the chemical. In these preliminary observations a small group of animals was studied in a variety of ways to include the widest possible scope of variables. Studies are now in progress to extend and confirm the findings.

DIAGNOSTIC AND THERAPEUTIC RADIOISOTOPES

Carcinoma of the Thyroid

Carcinoma of the thyroid has been a long-term interest of the Division. Current concepts of the disease have been altered significantly. A few years ago it was believed that only a minority of patients with this disease had lesions that would show any significant ability to concentrate the radioisotope, and for the rest, radioiodine was of no value. It has been found that in a majority of patients the lesions show at least some "uptake" of radioiodine. Even if this is not of a level to offer effective therapy, it may allow effective diagnostic studies. The principal reasons for this apparent change have been alterations in methods of study and improved equipment. In patients who have had a total thyroidectomy for carcinoma, large test doses of one-to-five millicuries are used. Efforts to locate lesions are made after most of the unbound isotope has been excreted, usually at least three days after the dose is given. Lesions formerly missed are now detectable with the improved Oak Ridge National Laboratory area scanner and the Division's linear scanner.

Encouraging results continue in patients with papillary and follicular carcinoma of the thyroid with out distant metastases. This involves, first, a total thyroidectomy and resection of enlarged lymph nodes without radical neck dissection, followed by test doses of radioiodine. Further surgery is carried out for areas of radioactivity found on scans. Surgery is given up if the functioning tissue cannot be located even with the surgical probe counter, or if the area of activity is nonresectable without excessive functional impairment; for example, lesions involving the larynx itself or foci at the site of entrance of the recurrent laryngeal nerve. If functional foci of tumor remain after all reasonable surgical attempts, therapeutic radioiodine is given. Until now none of the patients in this particular group has been found to have distant metastases or other evidence of failure referable to the omission of radical neck dissection. Several patients who have had radical neck dissections at other hospitals have been found to have residual tumor in lymph nodes on the side of the operation, as well as on the opposite side and near the midline.

New detection methods have presented some new problems. Patients previously believed to have "blank" necks by earlier scanning methods are now sometimes found to have foci of radioactivity. Sometimes these are not newly developing lesions but new detection of lesions that have been in existence. The "high-level" whole-bod counting setup has also revealed evidence of small amounts of functioning tissue in the retention curve patterns.

In addition, these areas of slight uptake, now detected by the large test dose and the more sensitive instrumentation, cannot always be eradicated completely by radioiodine therapy, even though clinical control of the disease may be satisfactory.

Development of Radioisotope Diagnostic Tests

The measurement of urinary hippuric acid exretion after oral or intravenous administration of sodium benzoate is Quick's well known liver function test. The analytical technique normally used in the test is time consuming and subject to certain inaccuracies. Use of a labeled benzoate would considerably simplify the analytical procedure. Iodine-131-labeled O-iodo-benzoic acid has been prepared by direct synthesis and by an exchange reaction. In vivo experiments in animals indicate, by the absence of any appreciable iodine-131 uptake in the thyroid gland, that the iodine bond is stable. Further studies will be carried out to determine whether this radioisotopic technique warrants trials in man.

Benzoic acid is detoxified and excreted in urine mainly as hippuric acid; a small portion is also excreted as benzoyl glucuronate. Other workers have reported that the benzoyl glucuronate excretion may be a more sensitive indicator of liver function than hippuric acid excretion. Preliminary work indicates that labeled hippuric acid and benzoyl glucuronate may be readily determined in the presence of each other through the use of counting and solvent extraction techniques.

TRACER AND BASIC BIOLOGICAL STUDIES

Antibody Synthesis by Human Cells

An in vivo tissue culture system has been developed for propagation of human cells and the study of their antibody-forming ability. This involves the use of a small plastic device shaped like a washer used on a garden hose. The two open sides can be closed by attaching sheets of a special fine-mesh "milipore" filter. This filter has holes in it about 1/7 the diameter of a red blood cell and thus will not allow cells to move in or out but will allow tissue fluids to diffuse freely. The procedure is as follows: Lymphatic or bone marrow cells are obtained from a patient at the time of surgery or by aspiration. These cells are placed in the capsule suspended in a liquid medium and a small amount of antigen is placed with them. The capsule is sealed and placed in the abdominal cavity of a mouse that has received a near lethal dose of radiation to prevent its own immunologic responses from being active. After a week to ten days, the capsule is removed and the liquid is studied for the presence of antibody. Serum also is obtained from the mouse as a control determination. In some of these experiments it has been possible to prove clearly that the human tissue in the small capsule produces antibodies in response to the antigen placed with them. In these cases, a serum agar diffusion procedure has shown the presence of human gamma globulin in the capsule, indicating that the antibody was not of mouse origin. The human gamma globulin could not be detected in chamber fluids that were negative for the presence of the antibody. Another proof that the antibody is not of mouse origin is that it is not detected in the serum of the host mouse. Additional studies have shown a marked uptake of tritiated thymidine by premitotic cells in the chambers after as long as 14 days of incubation in the host mouse.

Specific Activity in Radioisotopic Measurements

In a laboratory procedure designed earlier for nuclear medical te·ching, the goldfish proved convenient for illustrating the effect of specific activity on radioisotopic uptake. The model consisted of a series of dilutions of physiological saline containing equal amounts of tracer sodium-22 and widely differing amounts of total sodium. After placing a small goldfish in 200 ml of each dilution, the tracer remaining in solution was measured at intervals during two days.

The present model uses ten 3- to 4-inch goldfish in a 4-liter volume of liquid placed in a small aquarium designed for radioactive solutions. In comparative measurements with sodium-22, and chlorine-36, the sodium and chlorine tracers were used in similar series of sodium chloride dilutions, and radiophosphate (P^{32}) was used in analogous dilutions of phosphate buffer, pH 7. The sodium and the chloride tracers gave similar qualitative results, but sodium exchanged faster. In a series of 1/5, 1/50, 1/200, 1/500, 1/1000 physiological saline, the movement of tracer sodium into the tissues of the fish increased while decreasing concentration. For example, in a three-day study the uptake was less than 2% of the original tracer in the 1/5 dilution and more than 60% for the 1/1000 dilution. Expressed as millimoles of total radioactive and stable ion per kilogram of fish, the order of uptake was reversed. For example, the fish removed more than 30 millimoles of sodium per milligram in 2 days from the most concentrated pool, and less than 1 millimole in 5 days from the least concentrated pool. By comparison, the tracer phosphate gave less uniform results. Autoradiography, however, showed similar gradations for typical series with each of the three tracers.

METHODS

Small-Animal Linear Scanner: Calibration and Use

Numerous radioisotopes of possible diagnostic and therapeutic use have not yet been tried in patients. Such trials call for preliminary study in animals, and it is difficult to determine distribution patterns and excretion rates. External measurement of radioactivity in cross-sectional segments of an animal provides data on the internal behavior of a radioisotope. Although the information is incomplete, rapid screening for distribution and repeated measurements on the same animal offer advantages that are unavailable with destructive testing. The Division's small-animal linear scanner has been calibrated for iodine-131 in the rat and applied to verify thyroidectomy in animals used for metabolic studies. It has also proved useful with other selected radioisotopes, injected by various routes, including sodium-24, potassium-42, scandium-46, niobium-95 and cerium-144. Repeated scans at increasing time intervals enable rapid estimation of the changing distribution.

Quantitative C^{14} Assay of Thin-Layer Chromatography Plates

A fast and reliable technique was developed for recovering radioactive (carbon-14 and tritium) fats after chromatographic separation on thin layers of silicic acid. The procedure requires no elution steps, which makes it ideal for quantitative measurements in metabolic studies of complex fats isolated from tissues.

Apparatus for in vivo $C^{14}O_2$ Collection and Subsequent Scintillation Counting

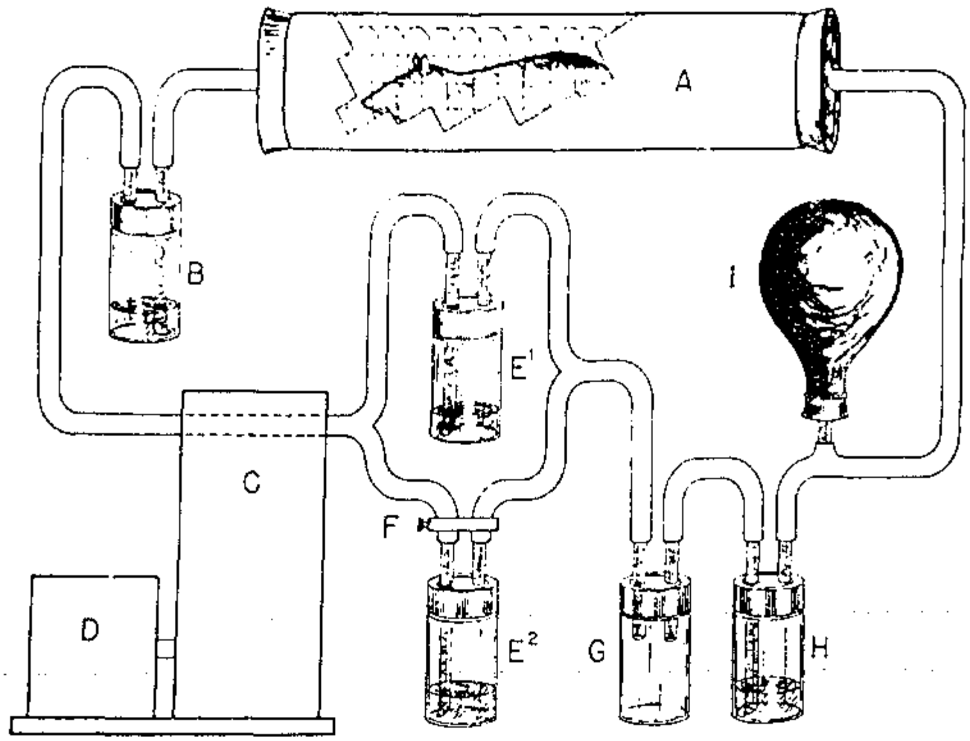
A convenient method for collection and radioactive assay of carbon-14 dioxide involving no transfer steps was developed to study the oxidation of C^{14}-labeled materials administered to small animals. The exit tube from the chamber was connected to a scrubber (B) containing 5 ml concentrated H_2SO_4 for removal of exhaled water. The exhaled gases were circulated through the system by the kneading action of a sigma motor pump (C,D) at the rate of 185 ml per minute. The carbon dioxide was collected in a liquid scintillation vial containing 4 ml of hydroxide of hyamine 10 x. Two such vials were connected to a Y tube (E^1 and E^2) with a pinch clamp (F) used for diverting the gas flow into only one of the vials. A filter paper disc was inserted around the delivery tube going into the hyamine to prevent spattering. The return system to the metabolism tube consisted of an empty vial (G) (to serve as a trap for preventing the entry of H_2SO_4 into the counting system), a vial containing concentrated H_2SO_4 (H) (to absorb any methanol evaporated from the hyamine), and a balloon (I) containing about one liter of oxygen. (See illustration on Page 22).

After allowing the expired gas to flow through a given vial for 15 minutes the flow to that vial was turned off and diverted to the second vial and the process was repeated. Ten minutes after cessation of flow to a vial, the filter-paper disc was slid off the delivery tube into the counting vial and 15 ml of scintillation cocktail (4 g PPO, 0.1 gPOPOP in 1 liter toluene) were added to the vial. The delivery tip was always rinsed with a portion of the cocktail. The contents of the vial were mixed and the radioactivity was measured with a Packard Tri-Carb liquid scintillation spectrometer (high voltage tap 5,10-70-100 windows). Recovery of radioactivity was tested by liberating a known quantity of $C^{14}O_2$ from $Na_2C^{14}O_3$.

The apparatus offers the advantage of permitting a large scale monitoring of the oxidation of carbon - 14 - labeled metabolites administered to small animals.

TRAINING

Preceptorship training continued, although at a somewhat reduced level from previous years, because of a scarcity of suitable candidates for the



Apparatus for collecting $C^{14}O_2$ (in vivo) for direct scintillation counting.

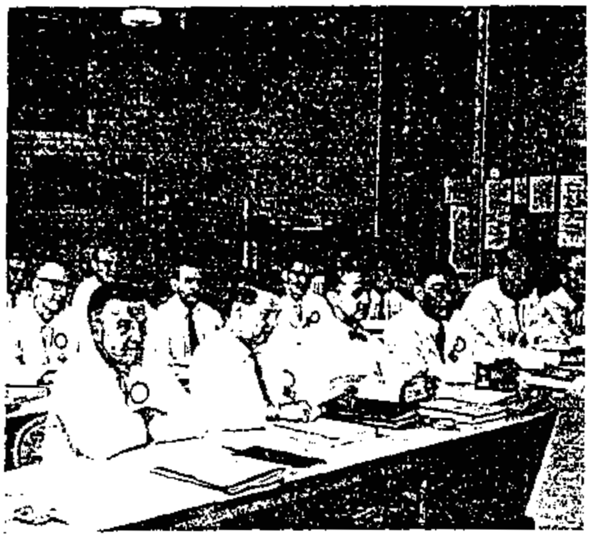
fellowship program. The short-term residency program was maintained and there have been, or are scheduled, six residents in radiology for three-month periods. Four medical students were at the Division during their off-quarter following their junior year, under sponsorship of the Abbott Student Fellowship in Nuclear Medicine. Visiting foreign scientists during the year include one from Japan, on a Damon Runyon Fellowship; one from the International Atomic Energy Agency (Thailand), and one from Germany on a Fellowship in Clinical Investigation. In addition, there is one advanced student from Japan under sponsorship of the Picker Foundation. Experience also was provided for seven college student trainees in the ORINS summer training program, and four research participants were assigned to the Division for the summer quarter.

TRAINING COURSES

Qualification courses for physicians were continued. Additional space permitted expansion to 24 participants in each session. Each three-week course is given in one-week sessions as Preclinical I, Preclinical II and Clinical III. The Clinical III week for one of these sequences is given at the Mayo Clinic. The scheduling of Preclinical I and II for residents was modified. These are given in continuous two-week sessions to eliminate the expense of one of the round-trip fares to Oak Ridge. With further experience in the laboratory sessions, it was found worth-while to modify some of the experiments. The experiment on specific activity and cationic exchange across a membrane was refined and enlarged. The refinements on these experiments are based on use in previous training courses. The aim has been to provide the most vivid and foolproof laboratory exercises to properly ground the participants in the clinical uses of radioisotopes.

A training device was designed and constructed to demonstrate the principle of operation of Dekatron tubes.

All the midget exhibits, "What Physicians Should Know About Radioisotopes," were completed and explanatory texts were printed. A draft copy of this material was bound for distribution and study. These 40 exhibits were reviewed at staff conferences. Thus a review of basic data was provided



Courses and seminars in the preclinical and clinical uses of radioisotopes are presented regularly at the Institute's Medical Division.

for the staff, and instruction was given to the visiting participants.

The special advanced course for the year was a five-day symposium entitled "Advances in Clinical Radioisotope Instrumentation." Sixteen guest speakers, experts in their field, from Oak Ridge and from institutions throughout the country provided lectures along with members of the Division staff.

The Division staff participated in other training activities. In cooperation with the Biology Division of the Oak Ridge National Laboratory, a workshop was presented on "Radioisotopes in Biomedical Research" for the Pathology Study Section of the National Institutes of Health. A two-day special seminar was presented for members of the staff interested hematology. Amoz Chernoff, University of Tennessee Memorial Hospital, and Alfred Kraus, University of Tennessee School of Medicine in Memphis, were the guest consultants. The discussion centered around special clinical hematologic patients seen in the Division during the year. The Division staff also took part in the Basic Course in Radioisotope Techniques given by the Institute's Special Training Division; the Armed Forces Medical Symposium at the Field Command DASA, Sandia Base, Albuquerque, N. M., and in a variety of symposia for medical societies. These meetings included the American Medical Association, Clinical Session, Denver, Colo.; Denison (Texas) Medical Society Postgraduate Seminar; Special Training Division Summer Teacher's Institute; North Carolina Medical Society; Postgraduate Symposium, Toledo Academy of Medicine; Colorado State Medical Society; Paducah (Kentucky) Medical Society. Staff members also participated in the Institute's Traveling Lecture Program.

PATIENT DAYS

July	327
August	370
September	382
October	504
November	486
December	340
January	310
February	332
March	392
April	483
May	401
June	367
Total Patient Days	4694
Average Per Month	391
Average Per Day	12.8

ISOTOPES USED BY MEDICAL DIVISION

Barium 133	0.4
Chromium 51	1.
Cobalt 57	0.22
Gold 198	1090.
Hippuran	3.
Iodine 125	2.
Iodine 130	55.2
Iodine 131	
Oriodide	4745.
Radiocaps	20.4
Rose Bengal	8.
Risa	21.25
Iron 59	0.5
Iron 59 (P)	2.10
Lanthanum 140	275.
Mercury 203	5.8
Phosphorus 32	290.
Rachromate	10.
Raolein	0.75
Sodium 22	0.75
Thulium 170	50.
Thymadine	0.5
Triomet	3.5

RESIDENT IN CLINICAL INVESTIGATION

Karl F. Hubner—Homburg/Saar, Germany

JAMES PICKER FOUNDATION FELLOW

Takashi Honda—Kanazawa City, Japan

ABBOTT STUDENT FELLOWSHIPS IN NUCLEAR MEDICINE

Frances Klinman—Woman's Medical College, Philadelphia, Pennsylvania

Michael G. Chen—University of Michigan, Ann Arbor, Michigan

Tom DiSilvio—Stritch School of Medicine, Chicago, Illinois

John A. Feemster—Meharry Medical College, Nashville, Tennessee

RESIDENT PHYSICIANS

Nathan T. Griscom—Massachusetts General Hospital, Boston, Massachusetts

Robert A. Nebesar—Massachusetts General Hospital, Boston, Massachusetts

James J. Pollard—Massachusetts General Hospital, Boston, Massachusetts

Abbott Miller—Massachusetts General Hospital, Boston, Massachusetts

Carl T. Stubblefield—Baroness Erlanger Hospital, Chattanooga, Tennessee

Harvey H. Grime—Baroness Erlanger Hospital, Chattanooga, Tennessee

MEDICAL DIVISION COURSES

Preclinical I for Residents, July 24-28, 1961	14 Participants
Preclinical I, August 21-25, 1961	19 Participants
Preclinical II for Residents, September 25-29, 1961	12 Participants
Advances in Clinical Radioisotope Instrumentation, October 23-27, 1961	33 Participants
Preclinical II, December 4-8, 1961	20 Participants
Clinical III, January 22-26, 1962	19 Participants
Preclinical I, February 19-23, 1962	24 Participants
Preclinical I for Residents, March 26-30, 1962	23 Participants
Preclinical II for Residents, April 2-6, 1962	20 Participants
Preclinical II, May 21-25, 1962	26 Participants

MEDICAL DIVISION CLINICAL CONFERENCES—1961

July 6: The use of I 132 to follow thyroid function after radioiodine therapy of hyperthyroidism—Ralph R. Cavalieri, head, thyroid clinic, U. S. Naval Hospital, Bethesda, Maryland.

July 10: Preliminary work on a whole-body counter designed for use with diagnostic and therapeutic dose levels—D. A. Ross, John C. Travis and Vichai Poshyachinda.

July 13: Midget exhibit no. 18—calibration—Marshall Brucer and Roger Cloutier.

July 17: Midget exhibit no. 22—the Geiger-Muller tube—Marshall Brucer and Roger Cloutier.

July 20: Specific radioactivity in tracer studies (goldfish)—G. C. Kyker.

July 24: Presentation of two cases receiving radioiodine therapy—B. W. Sitterson.

July 27: Discussion of the treatment of two patients with carcinoma of the thyroid—*Staff.*

August 3: Midget exhibit no. 21—the ionization chamber — Marshall Brucer and Craig Harris.

August 31: Midget exhibit no. 23—the scintillation crystal—Marshall Brucer and Craig Harris.

September 7: Case presentation—remission in acute leukemia after total-body irradiation without bone marrow infusion — D. A. White.

September 12: Case presentation—papillary carcinoma of thyroid —I 131 studies including whole body counting—*Staff.*

September 14: Midget exhibit no. 24—electronic circuits—Marshall Brucer and A. C. Morris, Jr.

September 21: Hematologic studies and autopsy findings in the black-necked tamarin—Nazareth Gengozian and Bill Nelson.

September 28: Chromium and iron studies in hematologic disorders—D. A. White and B. M. Nelson.

October 5: Midget exhibit no. 26—the spectrometer — Marshall Brucer and Craig Harris.

October 19: Midget exhibit no. 25—the scaler—Marshall Brucer and A. C. Morris, Jr.

October 26: Case presentations thyroid carcinoma—Staff.

November 2: Report on trip to South America—F. Comas.

November 9: Four-year study of cholesterol-lipid lowering agents in 20 diabetic patients—W. E. Cornatzer, professor of biochemistry, School of Medicine, University of North Dakota.

November 16: Case presentations—two patients with diagnostic problems in hematology.—Staff.

November 30. External counts of Cr^{51} and Fe^{59} — Mock spleen liver phantoms—Vichai Poshyachinda and Bill Nelson.

December 7: Cobalt-labeled vitamin B_{12} measurements — C. C. Lushbaugh, Los Alamos Scientific Laboratory.

December 14: Experience with I 131 at the Colombian National Cancer Institute, Colombia, South America—Efraim Otero.

December 21: Nuclear fallout—Roger J. Cloutier.

MEDICAL DIVISION CLINICAL CONFERENCES—1962

January 4: Chronic anemia associated with unexplained bleeding from the GI tract—David A. White.

January 11: Treatment of carcinoma of the maxillary antrum with multiple radioactive sources — Paul St. Aubin, Massachusetts General Hospital.

January 18: Three deaths from thyroid carcinoma—Bill M. Nelson.

January 25: The triiodothyronine *in vitro* uptake test — W. N. Tauxe, Mayo Clinic, Rochester, Minnesota.

February 1: Death from local recurrence of thyroid carcinoma—Bill M. Nelson.

February 8: Internal dose—Ray Hayes.

February 15: 1962 Modern Methods Analytical Symposium—G. C. Kyker.

March 1: Thin layer chromatography of bone marrow lipids—Fred Snyder.

March 8: Biochemical studies in homologous disease—Arthur L. Kretchmar.

March 22: Design problems in the low-background facility—D. A. Ross.

April 12: Plasmapheresis and leukocyte transfusion—Ralph Kniseley and Karl Hubner.

April 26: Antibody formation in diffusion chambers — Nazareth Gengozian.

May 3: Negative pi mesons—F. Comas.

May 10: Particle accelerators and more about pions — Roger Cloutier.

May 17: Whole body counter: Hot patients and warm patients, *status report—William D.* Gibbs.

May 31: Combined oral Fe^{59} absorption test and La^{140} study of GI transit time—Bill M. Nelson.

June 7: Continuous flow paper electrophoresis—Ray Hayes.

June 11: Principles of gel filtration—Bertil Aberg, department of clinical biochemistry, Royal Veterinary College, Stockholm, Sweden.

June 21: Somatic chromosome aberrations in irradiated human subjects—M. A. Bender, biology division, Oak Ridge National Laboratory.

June 28: Irradiated bone marrow lipids—Fred Snyder.

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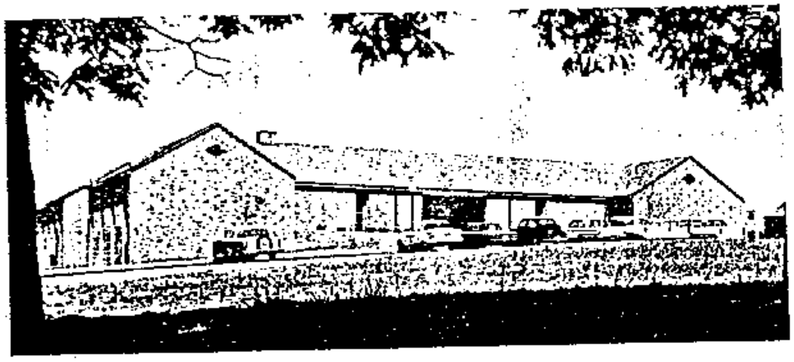
17th ANNUAL REPORT

Oak Ridge Institute of Nuclear Studies, Inc.

FOR THE YEAR ENDING JUNE 30, 1963



Exterior view of new Institute Library Building.

Library Department

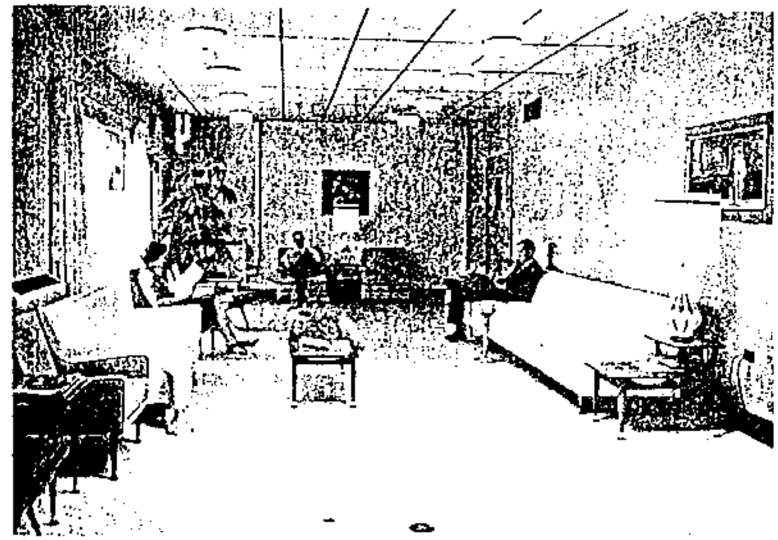
Designation of the Library as an AEC depository was made in November. This official recognition allowed the Library to make its collections and services available to the general public regardless of place of residence.

The Library completed its move to the new building in February. Located next to the Institute Central Administration Building, the new facilities offer an attractive atmosphere for library use and study. The increased space will allow an additional 10,000 volumes to be added to the 34,000-volume collection.

In cooperation with the Division of Technical Information Extension of the Atomic Energy Commission, the Library agreed to house and make available prepublication copies of unclassified conference papers appearing in Nuclear Science Abstracts. Future issues will specifically identify those papers deposited in the Institute Library. This program provides for the dissemination of conference papers well in advance of the published proceedings. Other libraries are encouraged to borrow this material on interlibrary loan, citing the specific Nuclear Science Abstracts entry with each request.

The Library is also acting as the intermediary in making Russian books held at DTIE available on interlibrary loan. These books are announced in the USAEC Translation List under the heading "Newly Received Russian Books." Material from the Library's collection was sent on loan to 39 states and 12 foreign countries.

Medical Division



Outpatient waiting room at Medical Division.

Since 1957 the Division has been studying patients with total-body irradiation. Since 1959 the Division has had available a special total-body irradiator having eight cesium sources which produces a very uniform dose distribution.

One group of patients has been treated with low doses, either 50 or 100 r, for chronic leukemia, lymphosarcoma, and related diseases. Most of the leukemias have been of lymphocytic type. In these patients a considerable amount of clinical benefit has been derived and this form of treatment appears to have practical usefulness. Each patient is studied for a period of at least six weeks after treatment, and unless essential to the patient's welfare, no other treatment is given that might alter the observations on clinical, hematologic, and biochemical parameters. Such relatively low-dose total-body irradiation has been used for many years in the treatment of these diseases. However, the unique thing about the Division's approach is the systematic evaluation of effects and the fact that treatment is given in a single dose. More commonly elsewhere, the treatment is divided into several smaller doses and this makes it somewhat more difficult to evaluate the time relationships of the responses. More than 40 patients have been treated at low doses over the whole period of the program.

Another group of patients has been treated at much higher doses. Most of these were treated before 1961 and a report has been made of the efforts to achieve marrow grafts on these patients. A few additional patients are being treated in an attempt to achieve remission in acute leukemia with a single dose in the neighborhood of 300 r without marrow-graft attempts.

Cell Preservation Storage Facility

In connection with the efforts to graft bone marrow it has seemed desirable to have a method of storing bone marrow and other tissues for long periods of time. Such a facility would make it possible to remove cells from a patient before giving marrow depressing treatment and to reinfuse them at a time when they are needed. Thus there would be no problem of genetic incompatibility. In another situation, the method can be used to build up a large number of cells from a single potential homologous donor, by making multiple collections over a period of months. The Division has chosen to use a device designed by the Linde Co., using liquid nitrogen and special equipment to control the rate of freezing. Samples of from 1 to 10 milliliters of bone marrow or leukocytes have been placed in sealed glass ampules, and samples of leukocytes up to a volume of 85 milliliters have been preserved in metal storage containers. The medium consists of a tissue culture medium or plasma with a final concentration of 10% dimethyl sulfoxide. Viability studies on the thawed cells have been made using tritiated thymidine, tritiated cytidine, and carbon-14-labeled uracil.

Among the tissues stored have been whole blood, leukocytes, bone marrow, suspensions of lymph node cells and splenic cells. These tissues have been obtained from patients with a variety of diseases, and from essentially normal patients. In a study of eight marrow samples stored for periods of one to three months, the average loss of nucleated cells was about 30% and the average reduction in number of cells taking up tritiated

thymidine and cytidine was 25 to 50%. The duration of storage did not appear to influence greatly the degree of these changes. Cells stored in this device have been used for the special diffusion studies in the immunology program.

Influence of Vascular Anoxia on Radiosensitivity

Studies were continued in rats to determine the radiosensitivity of bone marrow and tumor cells in the hind leg as influenced by anoxia. This is a part of the search for a method of enhancing radiation damage to tumors while minimizing the effect on normal tissues that lie in the same region. A method that would increase, even to a slight degree, the relative damage to the tumor, might greatly improve the results in cancer therapy. The anoxia was caused by clamping the arterial supply to the leg. Evidence of radiation damage was determined by measuring the time lag in recovery in normal levels of DNA synthesis by the marrow and tumor cells after exposure to irradiation. It was shown that for bone marrow the protective effect of anoxia has a value of 2; that is, it requires double the amount of irradiation to cause the same delay in recovery of DNA synthesis, while the protective effect of anoxia on the tumor has a value of 1.5. Although this effect may not apply to other combinations of normal tissue and tumors, it suggests that the induction of anoxia during radiotherapy might have definite value in increasing the relative effect on tumors.

Studies of Homologous Disease

The Division has carried on studies on the metabolic changes in homologous disease. These have been done in collaboration with Oak Ridge National Laboratory and Knoxville College. Homologous disease, also called secondary disease and foreign bone marrow disease, is a disorder that develops in animals that have been given large doses of irradiation followed by grafts of foreign cells. The animals survive the immediate effects of irradiation, but later, because of the presence of grafted foreign tissue, they develop weight loss (in spite of normal food intake), cessation of hair growth, and disorders of the lymphatic system. The outcome is usually death. The disease is of great importance because it represents a fundamental limitation on tissue graft therapy, it opens up fundamental immunologic problems, and it may be related to other wasting diseases.

One of the studies has brought out that in mice having homologous bone marrow grafts followed by so-called secondary disease, the nitrogen balance may be positive, even though there is rapid weight loss. This paradoxical result suggests that one aspect of the disturbance is an internal shift of nitrogen within the animal, possibly a shift of nitrogen from muscle and dietary intake into antigen and antibody proteins. Other possible explanations exist.

Another interesting observation in this work is that the lysozyme in the kidney is increased in animals with homologous disease. The function of this protein enzyme of kidney tissue is not known, but it may have an as yet unidentified role in immunologic responses. This enzyme is known to be increased in certain animals with malignant tumors and, in the Division laboratories, a striking rise in lysozyme was shown to be present in the kidneys of rats with Walker carcinoma S-256.

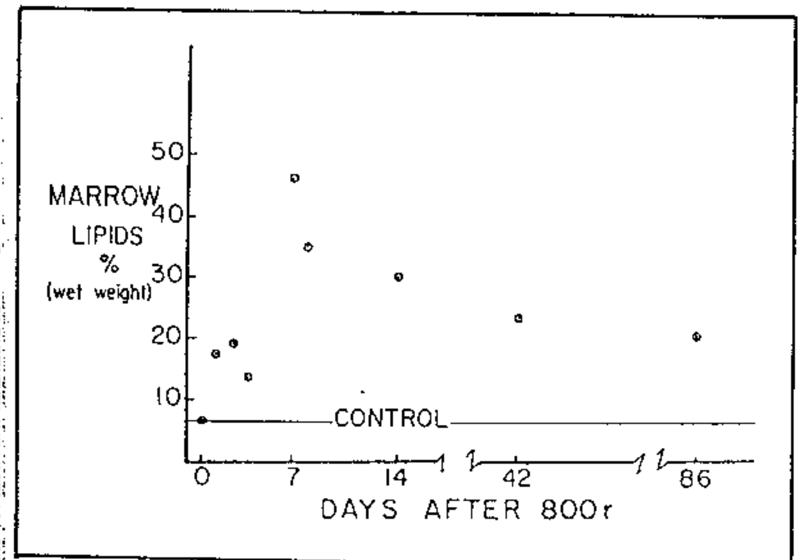
Further studies on the amino acid metabolism of mice with homologous disease show that the serine of liver, plasma, and muscle is reduced, even though the animals are eating normally. A striking and early decrease in serine concentration of the liver is seen. Serine levels of the plasma decrease somewhat more slowly, and those in muscle decrease still later. A speculative model of serine metabolism studied on an analog computer suggests that a marked increase in net loss of serine (either greatly accelerated utilization, blocked synthesis, or both) can explain the experimental results. This inbalance of serine metabolism appears to begin on about the fourth to sixth day after foreign marrow is injected. It emphasizes that the disturbances in the metabolism start very early, before the full clinical picture of homologous disease is present.

Bone Marrow Lipids in Animals Exposed to Total-Body Irradiation

It has been known for many years that after irradiation fat increases in the bone marrow. Hematologists have tended to consider this fat as unimportant filler, but recent information has emphasized the possible dynamic importance of it. Studies in rats performed at the Division have shown the time curve for increase in the bone marrow lipids after total body irradiation.

Peak values occur about one week after 800 r and the amount of fat decreases very slowly after this. The early lipid increase appears to occur as a function of dose. With the increase, there is some decrease in residue and a distinct decrease in water of the marrow. Thin-layer chromatography has been used to demonstrate that bone marrow lipids of rats are primarily triglycerides; gas-liquid chromatography demonstrated that palmitic and oleic acids account for more than 80% of the fatty acids present. Irradiation was shown to increase the triglycerides at the expense of water.

The mechanism for the increase in marrow lipid is not entirely clear. The absence of any change in the neutral glycerides of plasma suggests that increased transports of glycerides from other sites is probably not an important factor. At the present stage of the studies it appears that an increased bio-



Total lipids of bone marrow (wet weight) after 800 r total-body irradiation. Each value represents pooled samples from the following number of rats: 0 days=182 rats (range 5.5-9.3% for 7 pooled groups); 1 day=4 rats; 2 days=8 rats; 3 days=8 rats; 7 days=8 rats; 8 days=65 rats (range 33.1-46.3 for 5 pooled groups); 14 days=8 rats; 42 days=8 rats; 86 days=4 rats.

synthesis of triglycerides and reduced oxidation of fatty acids in the marrow are both involved in this fatty change that follows irradiation.

Glyceryl Ethers as Protective Agents Against Irradiation Leukopenia

The interest of the Division in bone marrow lipids naturally relates to the reports from other laboratories that glyceryl ethers tend to protect against certain irradiation effects, possibly even when not given until after the exposure. It has been shown at ORINS that glyceryl ethers are present in bone marrow, and the protective effect against irradiation depression of the bone marrow has been verified. The most definite results were obtained at relatively low or intermediate radiation doses.

Experimental Studies on a Small South American Primate

The immunology program of the Division has investigated the possibility of using a small monkey related to the marmoset, *Tamarinus nigricollis,* in laboratory studies. This project is under the sponsorship of the United States Air Force Aerospace Medical Division. Original studies included the definition of base line biological values for the new species, including the complete hematologic values, body temperature, body weight, and serum-protein components. The hematologic values for the tamarin are very similar to those of the rhesus monkey, which has been used more commonly in biological experimentation.

Studies with total-body irradiation indicated that the tamarins are relatively sensitive to irradiation, the LD_{50} being in the neighborhood of 200 r. Even 100 r produces profound alterations in the blood picture. Studies with a bacterial antigen P. tularense have shown that total-body irradiation produces a significant delay in antibody production and a decrease in the amount of antibody produced. However, even at doses of 400 r, which are lethal, there is a very significant antibody production before death.

Recently the activities in this tamarin project have been handicapped by lack of availability of healthy animals. It appears that the long-range promise for this project lies mainly in the possibility of developing a cage-bred and disease-free strain.

Negative-Pion Beam Project

The Oak Ridge National Laboratory has proposed building a 900 Mev cyclotron, based on the fixed-frequency alternating radiant principle, the outstanding feature of which would be a very high proton current of about 100 microamperes. If this project is approved it will offer a unique opportunity for studies of biological and medical effects of negative pions. Calculations indicate that large numbers of negative pions would be obtained from the interaction of the proton beam with a suitable target. These pions would be focused and brought into a special medical treatment room and used for irradiation of patients.

Several consultations took place with members of the Electronuclear Division of the Oak Ridge National Laboratory, with the aim of making preliminary plans for the design of the medical room. Several alternatives were discussed concerning the solid angle of pion collection from the target, ways and means of obtaining a flat beam, the question of focusing and bending magnets, and provisions for cross-fire irradiation. In addition, two Division staff members have visited several institutions where electron and proton accelerators are used for medical and biological work. They exchanged views with and obtained advice from people who have an interest in pion irradiation. Further consultations were held during a symposium on pi meson factories, at which they presented a paper on the possible use of negative pions in biology and medicine.

Medical Nuclides — Rare Earth Metals

Metabolic Studies — Until now increased fecal excretion of various heavy metals, which parallels increased intravenous dose, is undefined in mechanism or site. A study was carried out to make comparative measurements of the gastric, biliary, and segmented intestinal excretion of cerium and yttrium given to dogs. Both metals behaved similarly, and it was shown that there was direct alimentary excretion rather than biliary excretion. Excretion also occurs in the gastric segment of the tract as well as the usually defined excretory parts.

Previously, Division reports have been published establishing the observation that acute fatty infiltration of liver occurs regularly in rats after small intravenous doses (2 to 3.5 milligrams per kilogram) of any of the first five lanthanons. Elements in the series above samarium do not show this metabolic effect. A wide variety of hormonal factors and a few chemicals prevent the fatty liver. Although the transport of lanthanons remains unexplained, evidence supports the theory that stable soluble complexes with plasma proteins are formed, and the formation of a metal-enzyme complex could explain the acute metabolic effect. A variety of chelating complexes were prepared and a radiotracer of the element was used to show the distribution and excretion. It has been found that excretion increases and liver localization decreases with increased stability of the chelate in use. Fatty infiltration was sometimes prevented when the fraction in the liver was not reduced appreciably, a finding consistent with other preliminary evidence that the dominant fraction of the dose localized in the liver may not be the critical part of the dose causing the metabolic disorder.

Intralymphatic Administration of Radioisotopes to Lymph Nodes

Efforts to obtain radioisotopic localization of lymph nodes have continued because the need continues for radioactive preparations that can provide selective irradiation of lymph nodes involved in metastatic cancer. In addition, an agent that could localize in lymph nodes would be valuable as a tool in external scanning to establish the size and distribution of lymph nodes. Also, internal probing during a surgical procedure involving lymph-node dissection would be aided by such localizations of test compounds. Therefore, soluble preparations of gold-198, cerium-144, yttrium-90 chelates, etc., have been injected into lymphatics of dogs, after which observations have been made at prescribed intervals, including measurement of distribution and excretion, scintigrams by external scanning, and occasionally, radiography. It has been found that, in general, small chemical doses of yttrium-90 fail to localize adequately; they distribute like intravenous doses. Larger chemical doses localize better in lymph nodes. Ceramic microspheres containing Ce^{144} localize largely in the first lymph node of the stream. Results suggest that chelates of particle sizes somewhat smaller than Au^{198} colloid may be more suitable for lymph-node localization.

Radiation Dose to the Gastrointestinal Tract from Internal Emitters

The continuing program to assess the extent of dose variation to the intestinal tract from ingested emitters has progressed to the point where the following conclusions can be made:

1) Age of the subject does not seem to be an important factor even though intestinal motility tends to decrease with age.

2) A sizeable proportion of the population may have doses many times in excess of that assumed for the average "standard" man.

3) The dose experience of the group studied approximated that of a Gaussian distribution; the average dose, however, was approximately 70% greater than that predicted for the "standard" man with a long-life isotope.

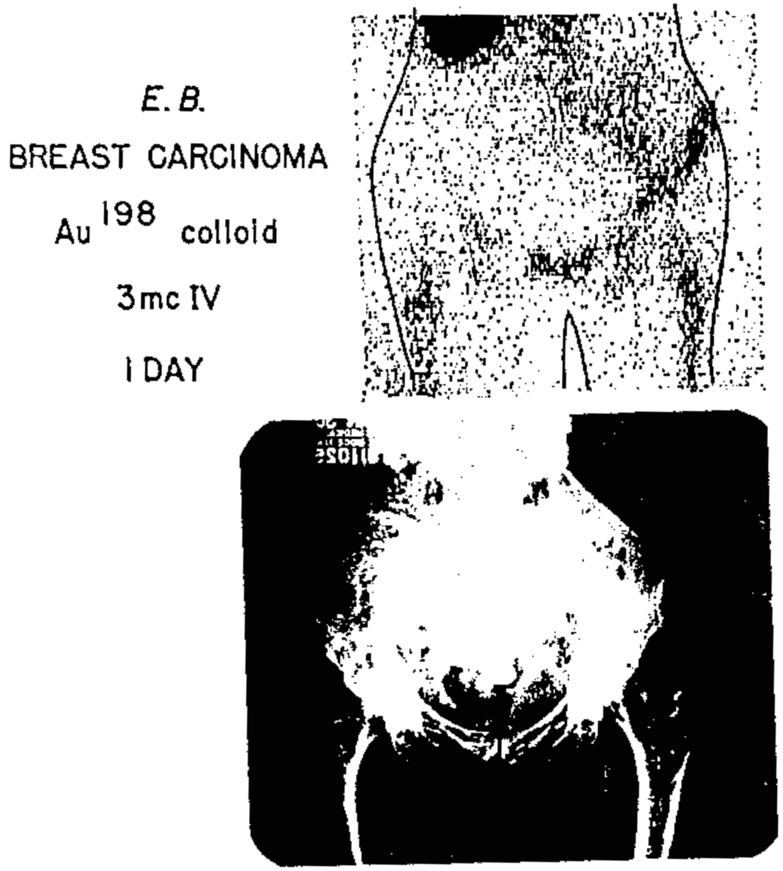
4) The route of entry of activity affects the dose received (whether through food at mealtime or through water between meals). If the results of this sampling are borne out in further studies, some adjustments in the assumptions for standard man may be in order.

Lanthanum-140 as a measure of the completeness of stool collections for all iron-59 absorption tests has been tested. Since lanthanum is not absorbed from the gastrointestinal tract, it can be given simultaneously by mouth with another tracer. Practically all the lanthanum-140 is accounted for in the feces, if collections are complete. Therefore, lanthanum can serve to detect incomplete stool collections in absorption studies of radioiron. It has been found, however, that the iron-59 will continue to appear in late stool specimens after virtually all the lanthanum has been recovered, suggesting that there may be transient binding of the iron to the mucosa of the intestinal tract.

Diagnostic and Therapeutic Radioisotopes

Carcinoma of the Thyroid — Interest continues in the long-term study of the use of radioiodine in the diagnosis and treatment of carcinoma of the thyroid. Experience has indicated some modifications in the technique of study which, along with improved scanning equipment, result in the finding of some degree of concentration of radioiodine in most lesions of thyroid carcinoma. In patients with this disease who have had a total thyroidectomy, doses from one to five millicuries of radioiodine are used in an effort to locate metastatic lesions. Such lesions are more likely to be found after most of the unbound isotope has been excreted and hence an interval of three or four days is allowed to elapse after the dose is given before the scanning is done, using the Oak Ridge National Laboratory procedure is done, using the Oak Ridge National Laboratory research scanner. Even though some of the lesions thus detected may not concentrate enough of the radioisotope to result in significant therapeutic effect, their detection permits better planning of other forms of therapy.

In patients in whom the metastatic disease is confined to the lymph nodes in the neck, local surgical excision is performed using the surgical probe counter. If subsequent scanning studies



Bone-marrow scan: local marrow lesion at site of metastases and radiotherapy.

show lesions still present, further local surgical resection is performed, unless the lesions are so located that surgery would result in excessive damage to adjacent normal structures. If lesions persist after all feasible surgery has been done, large doses of radioiodine are given for further therapy. This approach obviates radical neck dissection and results to date have been favorable.

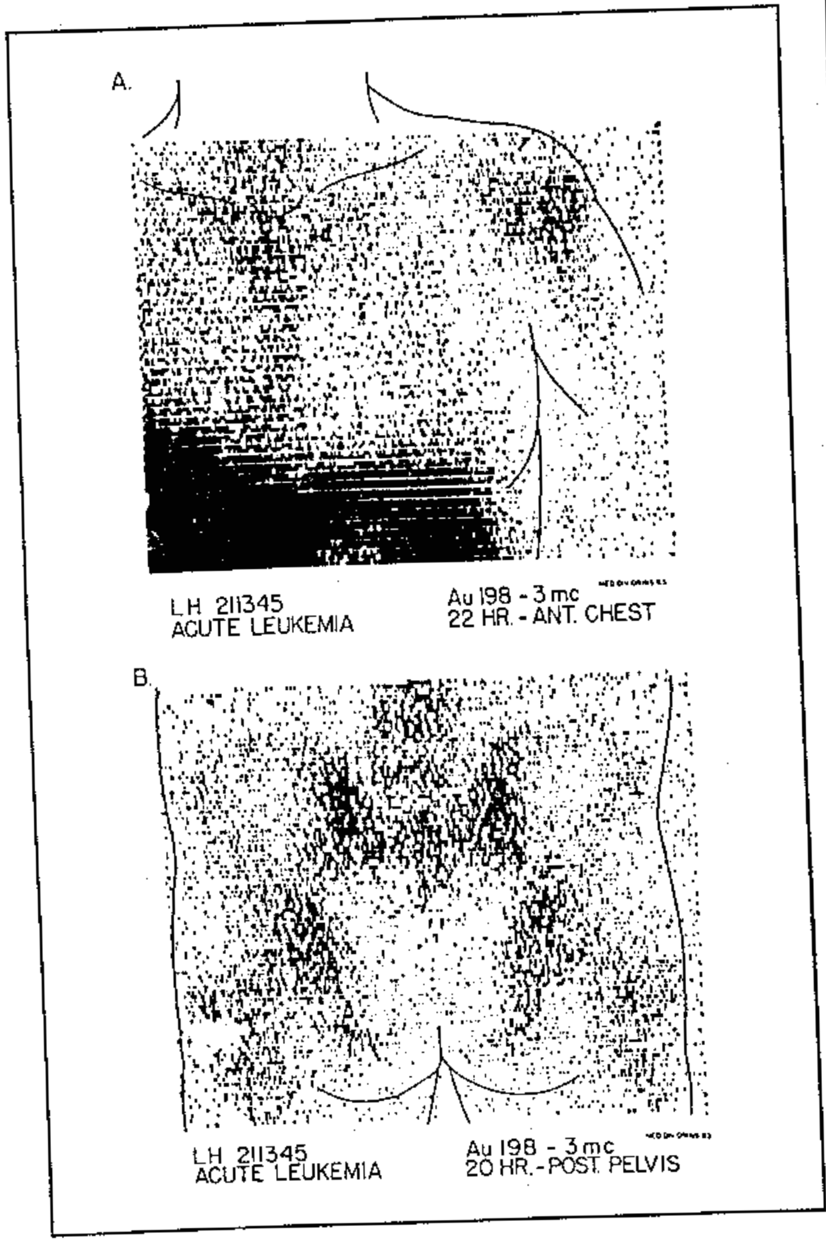
With the improvement in detection has come the realization that persisting lesions, concentrating radioiodine to only a slight degree but sufficient for their detection by scanning, may not receive significant therapeutic effect from the radioisotope. Thus these lesions cannot always be eradicated completely, although the clinical course of the disease may be controlled.

Clinical Scanning of Bone Marrow

The hematopoietic marrow is known to vary quantitatively from almost complete aplasia to extensive hyperplasia in different disease states. It is also known to be nonhomogenous at times. Heretofore, in clinical evaluation of the marrow we have been limited to surgical or needle biopsy and aspiration studies. Although these are useful, they provide limited information on the size and distribution of the hematopoietic organ. In earlier studies at the Division using colloidal Au^{198} intravenously, it was observed in autoradiographic studies that reticuloendothelial activity in the marrow coincided with the sites of hematopoietic activity. Using this observation and the ORNL research scanner, the Division has successfully demonstrated quantitative distributional changes of the bone marrow in patients with a variety of diseases.

Thirty-two series of bone marrow scans have been performed on 29 patients.

The series includes acute leukemia, 7; lymphosarcoma, 3; Hodgkin's disease, 4; metastatic breast carcinoma, 2; neoplasms without marrow involvement, 3; local radiation lesions to marrow, 2; polycythemia vera, 5; multiple myeloma, 3; miscellaneous, 3. The scans were made with three intravenously administered colloid preparations, the most satisfactory of which has been colloidal Au^{198}. Distinct pictures exhibiting the distribution of hematopoietic marrow have been obtained with the ORNL research scanner. Local lesions within the marrow organ have



Bone-marrow scan in patient with acute leukemia in partial control, showing normal or increased size of marrow organ.

been exhibited and confirmed by histologic studies. Variations in the size and distribution of the marrow organ have been exhibited in a graphic and nondestructive fashion, which has hitherto been impossible. Although the dose 1.5 to 3.5 millicuries is recognized to be in excess of that reasonable for persons with good prognosis, no ill effects have been demonstrated, and it is judged to be a safe procedure in patients who have poor prognosis. Bone marrow scanning using the present technique may be of considerable assistance to the investigator, and with improvement anticipated, the technique may find its place as a practical clinical procedure. When used in conjunction with area scans, linear scans are demonstrated to be of great usefulness and they give more quantitative information. Once interpretation of linear scans in relation to bone marrow function is clearly established, it will be possible to use small doses of the radioisotopes, for the linear scanner is a sensitive instrument. With appropriate accessory equipment, it gives promise of providing the most quantitative *in vivo* information on the distribution of radioisotopes important in hematologic diseases: Fe^{59}, Au^{198}, Cr^{51}, cobalt-labeled Vitamin B_{12}.

Tracer and Basic Biological Studies

Diffusion-Chamber Studies with Human Cells — Earlier at the Division it was found possible to produce antibodies against specific antigens in small, lucite, millipore diffusion chambers using human lymph-node tissue. Efforts have been made to define variables associated with induction of antibody formation against *Salmonella typhosa* antigen. The response has been found to be dependent upon (1) the dose of antigen relative to the number of human cells placed in the chamber, and (2) the number of cells placed in the chamber. Two different human serum proteins have been identified: gamma globulin and a macroglobulin, the latter identified tentatively by immuno-electrophoresis as beta 2-M protein. Cultivation of the cells in the chamber has shown a marked proliferative activity of lymphoid cells, as indicated by mitotic index and by incorporation of tritiated thymidine. There appears to be a definite correlation in thymidine incorporation, mitotic activity, and appearance of blast cells. Antibody formation has been obtained with human splenic cells, but several attempts with normal bone marrow and peripheral leukocytes have been negative thus far.

The slow-freeze liquid nitrogen controller and freezer established at the Institute has permitted long-term storage of viable human cells for these studies. Thus it has been possible to study in sequence, under various experimental conditions, the reactions of a single source of human immunologically functioning cells.

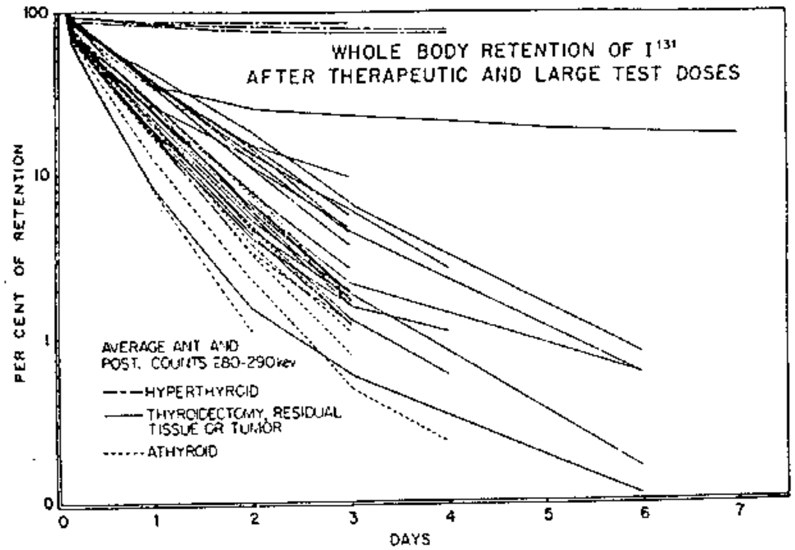
Methods

Aluminum Plates for Thin-Layer Chromatography — It has been found possible to substitute aluminum plates for glass plates in thin-layer chromatography, providing certain advantages in visualizing components of sulphuric acid charring. The aluminum plates are heated directly on a hot plate where the rate of heating is controllable while color changes are quickly and easily visible. This modification eliminates concern over breakage of the sample-containing plates. Aluminum sheet alloy 6061-T6 (4 millimeters thick) has been found to be satisfactory and sheets of it are cut to 20 x 20 cm. Silica Gel G and ethanol slurry is applied with a thin-layer applicator to make a 250 micron-thick layer.

Radiation Physics and Instruments

Hot Patient Counter — The instrument used for measuring whole-body retention of therapeutic levels of I^{131} in patients has been in routine use for more than one year. In the setting up of the instrument, studies with phantoms have shown that if patients are counted while supine and while prone, and these counts are averaged, accuracy is improved. In addition, if the proper portion of the I^{131} scatter spectrum is measured, rather than a primary gamma peak, the data reflect the amount of I^{131} present and are not affected by the distribution of the radioisotope within the phantom, or by the size of the phantom. In a variety of patients it has been shown that the assay values obtained by this method are essentially independent of the distribution of the isotope in the body.

Low-Background Whole-Body Counting Facility — Extensive testing of samples of concrete ingredients has been carried out during the past year in order to find ideal low-background shielding materials for the proposed high-sensitivity whole-body counter. The design has called for a uniquely low-level background and many of the materials that might ordinarily be



Retention of Iodine 131 in 33 patients for periods up to six days. All patients received either 5 millicuries or 100 millicuries.

useful as shielding contain unacceptable amounts of fallout products or natural radioactivity. Spectral analyses of a number of minerals and mineral products have been investigated, including the following: (1) limestone (largely calcium carbonate) from Oak Ridge; (2) dolomite (predominantly magnesium carbonate) from Knoxville and Mascot, Tennessee; (3) silica of two kinds — (a) natural sand from Caryville, Tennessee, and (b) crushed river-bed gravel, chiefly SiO_2 from Knoxville; (4) barite (naturally occuring barium sulfate) from the area around Sweetwater, Tennessee, and also from Del Rio; (5) olivine (iron-magnesium orthosilicates) from Balsam Gap, North Carolina; (6) iron slag (mainly iron silicate) from smelting works at Copper Hill, Tennessee; (7) iron sinters (clinker material nearly 70% iron) from Copper Hill, Tennessee; and (8) marble (calcium carbonate) from the Knoxville area.

Various samples of cement have also been assayed. Radioassay and spectral analysis have revealed that olivine sand from Balsam Gap, North Carolina, although an expensive material, has the least amount of interfering radioactivity. In making concrete even though a low aggregate in olivine is available, the Portland cements do have a higher content of radioactivity; therefore, it is necessary to enclose the cave structure with cold steel to shield from the activity in the cement. Assay of samples of shielding material have been in progress during the year.

Scanning Symposium — The Division presented its seventh Medical Symposium, "Progress in Medical Radioisotope Scanning," in collaboration with Oak Ridge National Laboratory. During the five-day meeting lectures were presented by 21 guest speakers. There were 158 participants. The field was covered comprehensively and the proceedings will be published in September 1963 through the Division of Technical Information Extension of the U.S. Atomic Energy Commission. It will include manuscripts of the formal papers, numerous illustrations, and edited transcriptions of the discussions. In addition to the daily session and evening reception, tours of the American Museum of Atomic Energy and informal workshops at the Medical Division were held in the evening.

Training

The Division continued to offer a variety of training experiences. Two foreign scientists have been here on International Atomic Energy Agency fellowships — one from Turkey and one from Thailand; one scientist from Japan on a James Picker fellowship; five Abbot fellowship medical students; two fellows in clinical investigation (one on assignment from U.S. Public Health Service); one postresident assistant in clinical investigation; seven summer trainees from the University Relations Division College Program; four summer participants from faculties of ORINS members schools; four short-term residents in radiology from Massachusetts General Hospital and one from Baroness Erlanger Hospital in Chattanooga.

In addition, the Division encouraged staff members to avail themselves of specialized training opportunities. Two staff members are working toward advanced degree at the University of Tennessee. One senior staff member attended a conference on Computer Science and Related Mathematics. The Division continued to cooperate with the Special Training Division in the courses offered in radioisotope handling and has assisted the Special Training Division in its program to provide qualification courses for physicians in radioisotope handling.

PATIENT DAYS

July	358	March	426
August	573	April	417
September	442	May	309
October	437	June	345
November	459		
December	309	Total Patient Days	4895
January	345	Average Per Month	408
February	475	Average Per Day	13.4

ISOTOPES USED BY MEDICAL DIVISION
(millicuries)

Carbon-14	1
Cerium-144	70
Chromium-51	20
Cobalt-57	0.0185
Gold-198	1281
Gold-199	8
Hippuran	2
Iodine-131	
Oriodide	3627
Radiocaps	426.76
Risa	12.75
Rose Bengal	5
Iron-59	1.750
Lanthanum-140	210
Mercury-197 (P)	5
Mercury-203	15
Phosphorus-32	190
Potassium-42	11
Racobalamin	0.005
Rose Bengal	0.300
Samarium-153	80
Selenium-75	0.5
Sodium-22	1.135
Thyroxine	0.58
Triolein	7
Triomet	5.500

RESIDENT IN CLINICAL INVESTIGATION
Karl F. Hubner — Homburg/Saar, Germany

JAMES PICKER FOUNDATION FELLOW
Takashi Honda — Kanazawa City, Japan

ABBOTT STUDENT FELLOWSHIPS IN NUCLEAR MEDICINE

Thomas V. DiSilvio — Stritch School of Medicine, Chicago, Illinois
Allan Lipton — New York University, Bellevue School of Medicine, Brooklyn, New York
John A. Feemster — Meharry Medical College, Nashville, Tennessee
Arthur E. Diamond — Tulane Medical School, New Orleans, Louisiana
William E. Rhodes — Meharry Medical College, Nashville, Tennessee

RESIDENT PHYSICIANS

Abbott Miller — Massachusetts General Hospital, Boston, Massachusetts
Melvin E. Clouse — Massachusetts General Hospital, Boston, Massachusetts
Lawrence C. Sack — Massachusetts General Hospital, Boston, Massachusetts
Richard J. Steckel — Massachusetts General Hospital, Boston, Massachusetts
William Massey — Baroness Erlanger Hospital, Chattanooga, Tennessee

POSTRESIDENT ASSISTANT IN MEDICINE

Donald W. Brown — Honolulu, Hawaii

VISITING SCIENTIFIC GUESTS

C. Lowell Edwards — U.S. Public Health Service, Staten Island, New York
Orhan Ternar — Turkey, International Atomic Energy Association Fellowship
Howard J. Cohn — Maimonides Hospital, Brooklyn, New York
Lars G. Ekman — University of Stockholm, Sweden
Makumkrong Wasanosomsithi — Thailand, International Atomic Energy Association Fellowship

MEDICAL DIVISION CLINICAL CONFERENCES — 1962

July 5: On the mechanism of action of neomycin in lowering serum cholesterol in humans — James G. Hamilton, Tulane University School of Medicine, New Orleans, La.
July 12: Aspartic acid in irradiation chimeras — Arthur L. Kretchmar.
July 19: Neutrons: their production and use in biology— Roger J. Cloutier.
August 9: Studies on tamarinus nigricollis — N. Gengozian.
August 16: I-131 colloidal albumin in scanning reticuloendothelial tissue — C. Lowell Edwards.

August 23: Influence of anoxia on the radiosensitivity of bone marrow and a tumor in the rat — F. Comas.
August 30: Some nutritional aspects of cerium induced fatty livers in rats — Isaac Miller, Department of Biochemistry, Meharry Medical College, Nashville, Tenn.
September 6: "Pyrodoxine responsive anemia" — David A. White.
September 13: Trip to Holland — N. Gengozian.
September 20: Report on second symposium on radioactivity in man — D. A. Ross and Ray L. Hayes.
September 27: Trip to Mexico — David A. White.
October 4: Gastrointestinal studies of cerium in dogs — Granvil C. Kyker.
October 11: Studies of myelogenous leukemia in the rat — William C. Moloney, Boston City Hospital.
October 18: Fatty acid oxidation in irradiated bone marrow — Fred Snyder.
November 1: (1) Liver uptake measurements and (2) I-131 thyroid uptake measurement survey in Japan — Hirotake Kakehi, Chief of Department of Radiology, Chiba University School of Medicine, Chiba, Japan.
November 8: Semi-conductor charged particle detectors and their applications — Bill Weiss, Chief Engineer of Detectors, ORTEC.
November 15: Clinical-pathologic conference — "obscure disorder involving bone marrow" — Bill Nelson.
November 29: Clinical-pathological conference—"an obscure disorder involving bone marrow — (R. C. 111278)" — Francis Jones, Pathologist, U. T. Memorial Hospital, Knoxville, Tenn.
December 6: Analog computer simulation of thyroid tracer study — Arthur L. Kretchmar.
December 13: Plasma clearance of Vitamin B_{12} in chronic myelocytic leukemia — David A. White.
December 20: "Health physics requirements for the study of transuranic elements in humans" — Roger J. Cloutier, Radiation Safety Officer.

MEDICAL DIVISION CLINICAL CONFERENCES — 1963

January 10: Demonstration of an analog computer program — Arthur L. Kretchmar.
January 17: Film "Recent advances in thin-layer chromatography" — made available by Orville Privett, Hormel Institute, University of Minn.
January 24: Leukemia treated with 6-mp and steroids (C.W. 111313) — Bill M. Nelson.
January 31: "Metabolic differences in certain metal chelates" — Granvil C. Kyker and John J. Rafter.
February 7: "Radioactive renogram using hippuran" — W. N. Tauxe, Division of Clinical Pathology, Mayo Clinic, Rochester, Minn.
February 14: "Self-organization in a natural plankton community" — Bernard Patten, Associate Marine Scientist, Virginia Institute of Science, Gloucester Point, Va.

February 21: "Geometry and background in the whole-body counter" — D. A. Ross.

February 28: "Scanning of intra-abdominal lymph nodes" — Donald W. Brown.

March 7: "Relative changes in radiosensitivity of tumor-bone marrow of the rat, under hypoxia" — F. Comas.

March 21: "Use of a medium scale digital computer for biomedical data: the IBM 1401 DPS" — J. E. Parham, Biology Division, Oak Ridge National Laboratory.

March 28: "Feedback inhibition in purine and pyrididine metabolism" — Edward Bresnick, Assistant Professor, Department of Biochemistry, Baylor University, Houston, Tex.

April 4: "Cellular amino acid transport" — Peter Rieser, Department of Physiology, University of Louisville, School of Medicine.

April 11: "Fluorometric determination of DNA" — Frank Comas.

April 18: "Laboratory design" — Roger J. Cloutier, Radiation Safety Officer.

April 25: "Course in mechanism of the ozonization of fatty acids" — Orville S. Privett, Professor of Chemistry, University of Minn.

May 2: "Analog computer simulation in medicine" — Alphonso Zermeno, Physicist, USAF School of Aerospace Medicine, San Antonio, Tex.

May 9: "Autopsy findings in tamarins after total body irradiation" — Bill M. Nelson.

May 16: "Radioisotopic localization by intralymphatic injection in dogs" — Takashi Honda.

May 23: "Intermittent steroid therapy in malignant lymphocytic diseases" — David A. White.

June 6: "The fate of injected I-131 deoxyuridine" — Karl Hubner.

June 13: "Enzyme kinetics" — D. G. Doherty.

June 20: "Clinical study of bone marrow using radioactive isotope scanning technique" — C. Lowell Edwards.

June 27: "Biological proof for two red cell subpopulations" — C. C. Lushbaugh, visiting scientist, Los Alamos Scientific Laboratory.

Special Training Division

A total of 333 scientists participated in courses in the techniques of using radioisotopes. This brought participation in Division courses to 5,219. Participants have come from each of the 50 states, the District of Columbia, Puerto Rico and 59 foreign countries.* Newly represented countries during the year were Costa Rica, Iraq and Uruguay.

Radioisotope Course

Some 148 scientists participated in the five basic courses in the uses of radioisotopes in research, industry, and engineering.

Lectures for both the research course and the engineering and industrial course cover such basic matters as nuclear theory, radiation detection, instrumentation, radiological safety, and the interaction of radiation with matter. In addition, lectures are given on radioisotope applications in both research work and industrial and engineering uses. Laboratory work and demonstrations acquaint the participants with techniques and instruments.

Summer

Sixteen participants attended the 4th Isotope Technology Institute for College Science Teachers. This institute was begun June 17, under the sponsorship of the National Science Foundation and the Atomic Energy Commission and those enrolled received National Science Foundation stipends.

Included with the 86th session of Basic Courses in the Use of Radioisotopes was an Institute in Advanced Radiation Biology under the sponsorship of the National Science Foundation. Twelve persons on National Science Foundation stipends attended this institute.

A summer institute in physics for small college teachers was begun June 17, with 20 National Science Foundation stipend holders attending.

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* *Argentina, Australia, Austria, Belgian Congo, Belgium, Brazil, Burma, Canada, Chile, Colombia, Costa Rica, Cuba, Denmark, Dominican Republic, Ecuador, Egypt, El Salvador, Finland, France, Germany, Great Britain, Greece, Guatemala, Iceland, India, Indonesia, Iraq, Iran, Ireland, Israel, Italy, Japan, Jordan, Korea, Lebanon, Luxembourg, Malaya, Mexico, Morocco, Nationalist China, Netherlands, New Zealand, Nigeria, Norway, Pakistan, Panama, Peru, Philippines, Portugal, Spain, Sweden, Switzerland, Thailand, Turkey, Union of South Africa, Uruguay, Venezuela, Viet Nam, and Yugoslavia.*

Participants in ecology course.

The second Institute in Radiation Ecology was begun June 10. Of the 22 persons participating, 20 were National Science Foundation stipend holders.

Other Courses

The first course in instrumental and chemical techniques of activation analysis was given September 24 through October 5, 1962, with 25 persons participating. This course was offered in an effort to extend the use of activation analysis in the life and physical sciences.

The health physics course was given to 18 participants from September 10 through November 16. The course is being offered in order to provide training to representatives of state and local governments who will be concerned with licensing and inspecting and is a part of the Atomic Energy Commission's program of encouraging state control of certain radioactive materials.

A highway engineering course was given to 25 participants March 11 through March 29. The goal of this course was to familiarize highway engineers with the application of radioisotope techniques in the field of highway engineering.

Medical Qualification Course

The medical qualification courses were designed to provide physicians with the minimal training necessary to acquire a license from the Atomic Energy Commission to use isotopes on patients. The courses are offered in three one-week sequences — basic, preclinical and clinical. During the year three basic, three preclinical and two clinical weeks were given. Forty-nine physicians participated.

Mobile Laboratory Program

The Mobile Laboratory visited 18 campuses of smaller colleges and universities in 14 states, and 269 students and faculty members took the course in isotope techniques. A total of 2,201 persons has taken this training to date.

Other Activities

Dr. Ralph Overman, Division Chairman, went to South America to complete arrangements for the International Secon-

Armed forces reserve unit members study devices used in the Special Training Division to provide instruction in industrial applications of radioactive materials.

dary School Program "Atoms at Work," conducted by the University Relations Division for the Atomic Energy Commission. He visited Lima, Peru; Santiago, Chile; Buenos Aires, Argentina; San Paulo and Rio de Janeiro, Brazil; Caracas, Venezuela; Panama, and Colombia. He spent three weeks overseas during April. He lectured extensively and visited various isotope laboratories in Japan, Thailand, India and in Europe.

"Nuclear Reactions," a film in the series "Understanding The Atom," was completed by Dr. Overman.

A book entitled *"Basic Concepts of Nuclear Chemistry"* authored by Dr. Overman was published by Reinhold Publishing Co.

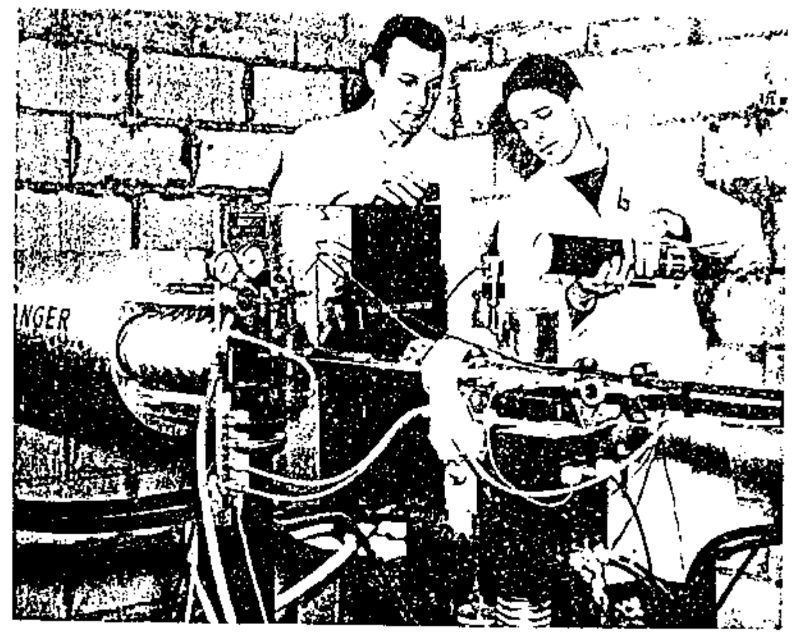
Dr. Elmer Nussbaum assisted the government of Singapore in establishing a radioisotope training program at the University of Singapore. The assignment involved organization of a training program and presentation of a major portion of the lectures in the first six-week course. Dr. Nussbaum participated as a cost-free expert, furnished to the International Atomic Energy Agency by the United States government. He was made available by the Institute on a cost-reimbursement basis with the Atomic Energy Commission. He also served as a member of a team of American scientists which, under the auspices of the National Science Foundation, visited the National Biological Institute in Bogar and Djakarta, Indonesia, to study and make recommendations regarding the use and the expansion of the Institute's facilities. He also discussed radioisotope training programs and research with organizations in Egypt and Austria.

Division Research

Dr. H. E. Banta carried out a research project on the oxygen content of rocks with Dr. A. Volbort of the University of Nevada. Fast neutrons and activation analyzers were used for the oxygen analysis.

Dr. Banta is also engaged in cooperative research work with Dr. James L. Carmon of the University of Georgia. In this project, mice are given measured doses of gamma or 14 Mev neutron or mixed irradiations. Any radiation effects are of interest but genetic effects are the ones receiving most attention.

A research project headed by Dr. Elizabeth Rona was initiated on the geochronology of marine sediments. This is con-



Neutron generator used at Special Training Division.

cerned with the dating of sedimentation and the development, particularly in the Gulf of Mexico basin, of techniques to form the basis of training for members of oceanographic departments and institutes in nuclear methods applicable to oceanography. Methods were developed for separating thorium and protactinium from sediments based on solvent extraction and on ion exchange techniques. Very thin samples were prepared by an electroplating method for counting.

Oak Ridge Radioisotope Conference

Dr. Overman served as joint chairman of the Oak Ridge Radioisotope Conference held at Gatlinburg, Tenn., April 1 - 3. The following papers were presented by Special Training Division personnel during the conference: "An Alpha Gauge System for the Continuous Measurement of Gas Density, Gas Pressure and Film Thickness," by H. H. Ross and R. P. Gardner; "Single Sample Radiotracer Technique for Determining Stream Flow Rates" by Robin Gardner and J. W. Dunn, III; "Diffusion of

Radioactive Gases Through Membranes" by Elmer Nussbaum; "A Wide Band-Pass Transistorized Ratemeter for Alpha Gauge Measurements" by M. C. Kopp, R. P. Gardner, and H. H. Ross; and "Liquid Scintillation Counting of Iodine 129 and Iodine 125" by Roger E. Yerick and H. H. Ross.

PARTICIPANTS — MEDICAL QUALIFICATION COURSES

Basic
October 8-12, 1962

Abrams, Julian E. .... Trinity Memorial Hospital, Cudahy, Wisc.
Bridgens, James G. .... St. Joseph Hospital, Kansas City, Mo.
Capo, James P. .... Stewart-Lakewood Clinic, Atlanta, Ga.
Crain, R. C. .... East Tennessee Baptist Hospital, Knoxville, Tenn.
Daniel, Gerald L. .... Central Intelligence Agency, Washington, D. C.
Eisenstaedt, Werner F. .... Chicago, Ill.
Gardner, Morris D. .... Scott and White Clinic, Temple, Tex.
Gatzimos, C. D. .... Logansport, Ind.
Grady, Edgar D. .... Atlanta, Ga.
Hornberger, Robert B. .... Georgia Baptist Hospital, Atlanta, Ga.
Lukash, Leslie .... Meadowbrook Hospital, Hempstead, N. Y.
Metzger, Russell C. .... Springfield, Ohio
Ternar, Orhan .... Istanbul University, Istanbul, Turkey
Webster, Robert M. .... Princeton Hospital, Princeton, N. J.

Basic
April 22-26, 1963

Capo, James P. .... Stewart-Lakewood Clinic, Atlanta, Ga.
Childers, John H. .... Dallas, Tex.
Coe, Herbert S. .... Buffalo, N. Y.
Eperjessy, Ernest Z. .... Windber Hospital, Johnstown, Pa.
Fleshler, Bertram .... Cleveland Metropolitan General Hospital Cleveland, Ohio
Horowitz, Herbert I. .... Cornell Medical Center, New York, N. Y.
Jackson, George L. .... Harrisburg Polyclinic Hospital Harrisburg, Pa.
Kaye, Donald .... Cornell University Medical College, New York, N. Y.
Keppler, Charles B. .... Sewanee, Tenn.
Lipo, Robert F. .... Veterans Administration Center, Wood, Wisc.
Lovice, Harris .... Baltimore, Md.
Lukash, Leslie .... Meadowbrook Hospital, East Meadow, N. Y.
Miller, Robert H. .... Kenmore Mercy Hospital, Buffalo, N. Y.
Nash, Gerald K. .... Shenango Valley Osteopathic Hospital, Farrell, Pa.
Resto, Manuel .... Wayne County General Hospital, Eloise, Mich.
Wallace, Keene M. .... Harrisburg Polyclinic Hospital, Harrisburg, Pa.
Weatherby, Marvine .... Dallas, Tex.

Basic & Preclinical
March 18-29, 1963

Berken, Arthur .... Bronx Municipal Hospital Center, Bronx, N.Y.
Berry, D. H. .... Washington University School of Medicine, St. Louis, Mo.
Carman, James W. G. .... United States Air Force Hospital, San Antonio, Tex.
Cummings, Patrick W .... Saint Anthony Hospital, Louisville, Ky.
Elliott, William E. .... United States Air Force Hospital, San Antonio, Tex.
Frazier, Horace M. .... Meharry Medical College, Nashville, Tenn.
Guyton, James R., Jr. .... Knoxville, Tenn.
Hampel, Donald C. .... Veterans Administration Center, Wood, Wisc.
Heidorn, G. H. .... Minot, N.C.
Lawrow, John W. .... Minneapolis, Minn.
Malvin, Harry H. .... United States Air Force Hospital, San Antonio, Tex.
McCaughey, Donald J. .... Veterans Administration Hospital, Columbia, S.C.
McGrath, James Ellis .... Bryn Mawr Hospital, Bryn Mawr, Pa.
Slivko, Benjamin .... Veterans Administration Hospital, Brooklyn, N.Y.
Tourney, Robert L. .... Birmingham, Ala.
Wasson, Richard D. .... Public Health Service Hospital, New York, N.Y.

Preclinical
December 3-7, 1962

Bridgens, James G. .... St. Joseph Hospital, Kansas City, Mo.
Crain, R. C. .... East Tennessee Baptist Hospital, Knoxville, Tenn.
Daniel, Gerald L. .... Central Intelligence Agency, Washington, D.C.
Eisenstaedt, Werner F. .... Chicago, Ill.
Gardner, Morris D. .... Scott and White Clinic, Temple, Tex.
Gatzimos, C. D. .... Logansport, Ind.
Grady, Charlotte .... Atlanta, Ga.
Grady, Edgar D. .... Atlanta, Ga.
Harshman, James A. .... St. Joseph Hospital, Kokomo, Ind.
Hornberger, Robert B. .... Georgia Baptist Hospital, Atlanta, Ga.
Metzger, Robert B. .... Springfield, Ohio
Petty, Frederick C. .... Memorial Hospital, Clarksville, Tenn.
Rayhill, Edward A. .... Grand Island, N.Y.
Ternar, Orhan .... Istanbul University, Istanbul, Turkey

Preclinical
May 20-24, 1963

Capo, James P. .... Stewart-Lakewood Clinic, Atlanta, Ga.
Childers, John H. .... Dallas, Tex.
Coe, Herbert S. .... Buffalo, N.Y.
Eisenstaedt, Werner F. .... Chicago, Ill.
Eperjessy, Ernest Z. .... Windber Hospital, Johnstown, Pa.

Horowitz, Herbert I. .... Cornell Medical Center, New York, N.Y.
Jackson, George L. .... Harrisburg Polyclinic Hospital, Harrisburg, Pa.
Kaye, Donald .... Cornell University Medical College, New York, N.Y.
Keppler, Charles B. .... Sewanee, Tenn.
Lipo, Robert F. .... Veterans Administration Center, Wood Wisc.
Lovice, Harris .... Baltimore, Md.
Lukash, Leslie .... Meadowbrook Hospital, East Meadow, N.Y.
Miller, Robert H. .... Kenmore Mercy Hospital, Buffalo, N.Y.
Nash, Gerald K. .... Shenango Valley Osteopathic Hospital, Farrell, Pa.
Resto, Manuel .... Wayne County General Hospital, Eloise, Mich.
Weatherby, Marvine .... Dallas, Tex.

Clinical

February 4-8, 1963

Bridgens, James G. .... St. Joseph Hospital, Kansas City, Mo.
Crain, R. C. .... East Tennessee Baptist Hospital, Knoxville, Tenn.
Daniel, Gerald L. .... Central Intelligence Agency, Washington, D.C.
Derian, Paul S. .... University of Mississippi Medical Center
Ehrenpreis, Bernard .... Miami Beach, Fla.
Gardner, Morris D. .... Ogden, Utah
Gatzimos, C. D. .... Logansport, Ind.
Grady, Charlotte .... Atlanta, Ga.
Grady, Edgar D. .... Atlanta, Ga.
Harshman, James A. .... St. Joseph Hospital, Kokomo, Ind.
Hornberger, Robert B. .... Georgia Baptist Hospital, Atlanta, Ga.
Marks, Jack .... Columbus, Ohio
McCowan, John P. .... Public Health Service Hospital, Baltimore, Md.
Metzger, Russell C. .... Springfield, Ohio
Mundy, Elbert J., Jr. .... Veterans Administration Hospital, Nashville, Tenn.
Petty, Frederick C. .... Memorial Hospital, Clarksville, Tenn.
Rayhill, Edward A. .... Grand Island, N.Y.
Ternar, Orham .... Istanbul University, Istanbul, Turkey
Webster, Robert M. .... Princeton Hospital, Princeton, N.J.

Clinical

June 17-21, 1963

Blaschke, John A. .... McBride Clinic, Oklahoma City, Okla.
Capo, James P. .... Stewart-Lakewood Clinic, Atlanta, Ga.
Childers, John H. .... Dallas, Tex.
Coe, Herbert S. .... Buffalo, N.Y.
Cummings, Patrick W. .... Saint Anthony Hospital, Louisville, Ky.
Eisenstaedt, Werner F. .... Chicago, Ill.
Eperjessy, Ernest Z. .... Windber Hospital, Johnstown, Pa.
Keppler, Charles B. .... Sewanee, Tenn.
Lingquist, M. F. .... Divine Redeemer Memorial Hospital, South St. Paul, Minn.
Lukash, Leslie .... Meadowbrook Hospital, East Meadow, N.Y.

Miller, Robert H. .... Kenmore Mercy Hospital, Buffalo, N.Y.
Nash, Gerald K. .... Shenango Valley Osteopathic Hospital, Farrell, Pa.
Niznik, Theodore T. .... St. Josephs Hospital, Baltimore, Md.
Sahler, Otto D. ... Mary Imogene Bassett Hospital, Cooperstown, N.Y.
Sherman, Abraham A. .... Bronx, N.Y.
Stinson, James C. .... Scott & White Clinic, Temple, Tex.

RADIOISOTOPE TECHNIQUE COURSES — 86TH SESSION

August 6-September 14, 1962

Courses A, B, and D (Aug. 6-Sept.14)

Allen, John R. .... Union College, Barbourville, Ky.
Cronin, Rev. Richard T. .... Society of Jesus, Toronto, Ontario, Canada
Gellenbeck, Sister Mary Mercy .... Mercy College, Detroit, Mich.
Giger, Karl .... Zurich, Switzerland
Lin, Chin Shin .... Taiwan, China
Mandel, Morris J. .... Wright-Patterson Air Force Base, Ohio
Perez, Jerome J. .... Fairfield University, Fairfield, Conn.
Quejada, Juan E. .... University of Philippines, Quezon City, Philippines
Scaglione, Peter R. .... Columbia University

Courses A, C, and D (Aug. 6-Sept. 14)

Chmielowiec, Frank V. .... Western Electric Company, Chicago, Ill.
Pyevich, Eli .... Ordinance Weapons Command, Rock Island, Ill.

Courses A and B (Aug. 6-31)

Bateman, John V. .... Turrialba, Costa Rica
Boada, Jose J. .... Caracas, Venezuela
Brown, Donald W. .... Oak Ridge Institute of Nuclear Studies
Castro, Victoria A. .... Manila, Philippines
Danti, August G. .... Northeast Louisiana State College, Monroe, La.
Dialameh, G. Hossein .... University of Pittsburgh
Dietrich, Felix M. .... Sripps Clinic & Research Foundation, LaJolla, Calif.
Fuerst, Robert .... Texas Woman's University
Gary, Julia T. .... Agnes Scott College, Decatur, Ga.
Goldwein, Manfred I. .... University of Pennsylvania
Green, James W. .... Rutgers University
Huang, Siong Kee .... Singapore, Malaya
Jimenez, Eduardo .... Turrialba, Costa Rica
Joiner, Jasper N. .... University of Florida
Khan, Parvin N. .... Bombay, India
Larson, A. D. .... Louisiana State University
Ljinsky, William .... Chicago Medical School
Miller, Abbott .... Oak Ridge Institute of Nuclear Studies
Mohammed, Khairi H. .... Republic Hospital, Bagdad, Iraq
Orth, Ronald E. .... University of Kentucky

Board of Directors of The Institute

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ANNUAL REPORT

Oak Ridge Institute of Nuclear Studies, Inc.

FOR THE YEAR [illegible]

Participating in the dedication ceremonies of the new Library Building were, from left, Harold T. Byck, Chairman of the Information and Exhibits Division; Paul M. Gross, President of the Institute; S. H. Wender, Chairman of the Institute Council; J. Louise Markel, Head, Library Department; William G. Pollard, Executive Director of the Institute; and S. R. Sapirie, Manager, Oak Ridge Operations, U.S. Atomic Energy Commission.

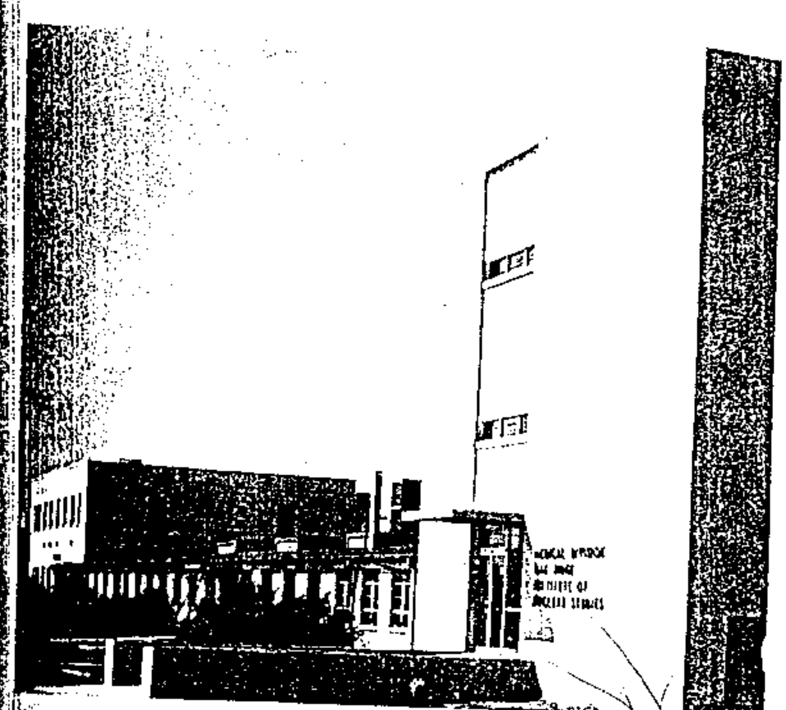
The purpose of the seminar was to acquaint these librarians with Institute Library facilities. To further encourage use of its facilities, the Library also prepared and distributed an information brochure and met with several groups of educators to explain the services available. Information about the Library was furnished to the National Referral Center in Washington, D. C., a clearinghouse for specific information requests throughout the United States.

Medical Division

The Medical Division conducts one of the nation's major programs in the medical uses of radioactive materials. This interrelated program includes clinical and preclinical research, medical physics and training. The Division operates a 34-bed hospital in connection with its clinical research.

Studies on Radiation Effects

Ninety patients have now been treated in the total-body irradiation program. As part of this program, a special facility with eight cesium-137 sources is used to produce uniform dose distribution.



View of the facility of the Institute's Medical Division.

Doses have ranged from 50 r to 900 r exposures. Most of the recent work has focused on the low-dose group, given either 50 r or 100 r, in a single exposure at a dose rate of 1.4 r per minute during this past year. Selected patients have received 300 r. Hematologic, biochemical and clinical observations have been made using a standard protocol.

Summary evaluations of the responses have been made in the following categories: 50 r in chronic lymphocytic leukemia; 50 r in chronic myelocytic leukemia; 100 r in lymphosarcoma. The overall results of low dosage, total-body irradiation treatment to patients with chronic leukemias and lymphosarcoma have been gratifying. The findings suggest that therapeutic benefits from 50 r to 100 r total-body irradiation are entirely comparable with those obtained with more conventional forms of treatment.

Changes in Frequency Distribution of Red Cell Volumes in Disease

Electronic equipment has become available for determining the number of suspended particles in a solution, and this has been applied to counting red and white blood cells much more precisely than previously possible. Using this equipment with a 400-channel pulse-height analyzer, a facility has been developed at the Division to measure the volumes of red and white blood cells. Frequency distribution curves can be produced quickly in a 100-channel sequence of narrow windows. Investigations are in progress to determine the frequency distribution profiles in health and in a variety of hematologic disorders. Studies are also being done on the sequential changes produced by total-body irradiation and other forms of therapy, such as chemotherapy for malignant tumors.

The frequency distribution profile of erythrocyte sizes determined with high aperture current on a saline suspension of red blood cells conveniently separates young cells from old ones because the young ones do not crenate as do the old ones. A bimodal frequency distribution curve results. Studies in progress show that this bimodality is lost in clinical situations where red cell production is absent; and the relative proportions of the two modal sizes change in relation to erythropoietic activity. Deficiency of iron or essential vitamins like B_{12} can cause the production of other modal sizes of cells, resulting in a trimodal curve of diagnostic usefulness.

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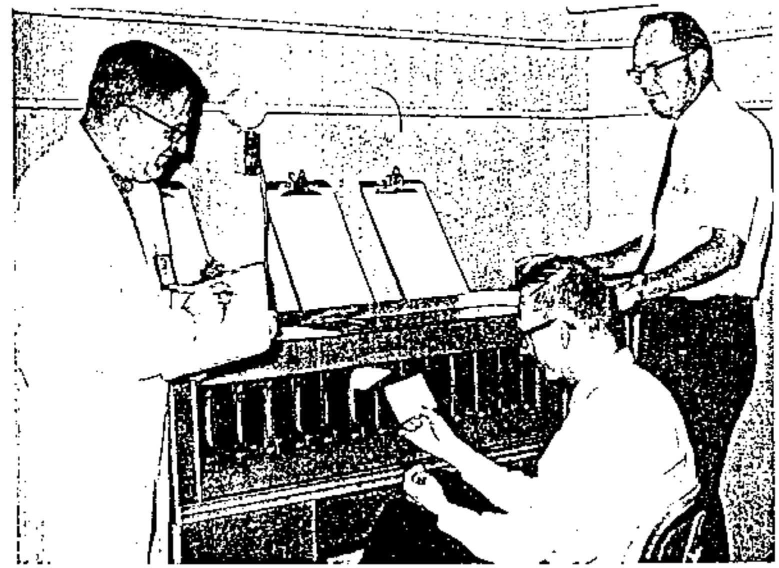


Staff members use a card sorter which is part of the data retrieval and computer equipment available for handling medical data.

Lipid Metabolism and Radiation

This program has been concerned primarily with lipid metabolism in the bone marrow. Hematopoietic areas of bone marrow contain, in addition to the various precursors of the cells which circulate in the blood, a considerable amount of fat. Under certain circumstances the amount of adipose tissue increases or decreases more or less as a reciprocal of the changes in hematopoiesis. Therefore, it is involved in a major metabolic process; and elucidation of the mechanism of fat cell formation in the bone marrow, especially that resulting from total-body irradiation and the effects of these accumulated lipids on cell repopulation, are major objectives of this work. A smaller portion of the program is devoted to evaluating fats as radioprotective agents because glyceryl ethers, normal constituents of hematopoietic tissue, are found to lessen the leukopenia observed in rats exposed to total-body irradiation.

During this past year, detailed assays have been made on lipids in the bone marrow of a variety of species, including the chimpanzee, tamarin, monkey, human, guinea pig, rat, rabbit, dog, minipig, sheep and steer. Metabolic studies have been carried out using carbon-14-labeled precursor compounds, and it appears that the major effect of irradiation on bone marrow lipid metabolism is to stimulate esterification that results in the deposition of newly formed triglycerides and to depress fatty acid oxidation.

To study the metabolic fate of orally administered glyceryl ethers, organic synthesis of carbon-14 and tritium-labeled batyl alcohol was carried out in collaboration with a summer research participant. Another significant achievement in this area was the development of a method for higher resolution radioassay of thin-layer chromatography plates. The apparatus was designed and built in the Institute's Technical Services Department. It permits automatic removal of thin segments of radioactivity from the plates and recovery of the sample into counting vials. Consequently, high resolution (1 mm) zonal scans of thin-layer plates permit separation of sharp peaks and, hence, separation of individual lipid compounds.

Amino Acid Metabolism and Irradiation

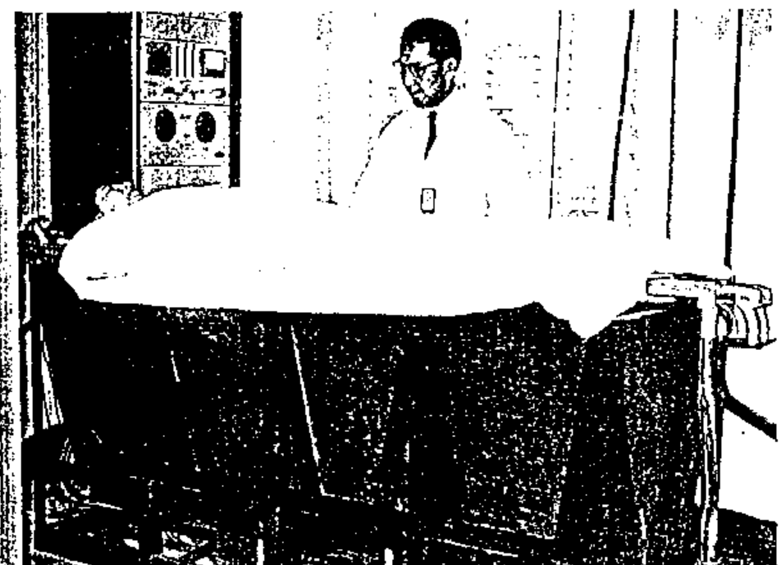
The Division has studied metabolic changes related to irradiation and to homologous disease, an immunologic phenomenon that is seen in animals following a successful homologous graft of bone marrow. In cooperation with the Biology Division of Oak Ridge National Laboratory, the Division has studied lysozyme activity in radiation chimeras. Striking changes in lysozyme activity in homologous bone marrow chimeras have been observed. A close time relation among liver weight, kidney weight, liver aspartic acid concentration, and lysozmye activity in kidney was observed; all increased 7 to 14 days after irradiation. Treatment with homologous bone marrow cells suggests that all are related to the same underlying metabolic alteration in the host, presumably triggered by the immunologic interaction of the graft and host.

In another study, analyses were made with respect to water content, RNA and DNA concentration in the livers of irradiation chimeras. Since the liver weights have been observed to be increased in irradiated mice given foreign bone marrow cells, the results here are consistent with the idea that proliferating hematopoietic cells require precursors of nucleic acid that are synthesized in some other organ, presumably in the liver.

The previous finding that animals with homologous disease have a positive nitrogen balance, despite weight loss and evidence of homologous disease, led to an experiment to determine whether significant shifts occur in the nitrogen content of various compartments in these animals.

Systems Biology Project

Increased attention has been given to the mathematical bases of use in describing any biological system. An analog computer has been acquired, and two "visiting scientists" have been invited to spend the next year at the Division working in this area. The goal of the project is to develop hypotheses concerning the position, movement, change or interplay of elements and compounds that are taking part in a dynamic metabolic process. Analog models are being developed which can then be tested by planned experiments, and the models suggest the most economical way of testing the validity of hypotheses.



Patient being counted on the medium-level whole-body counter.

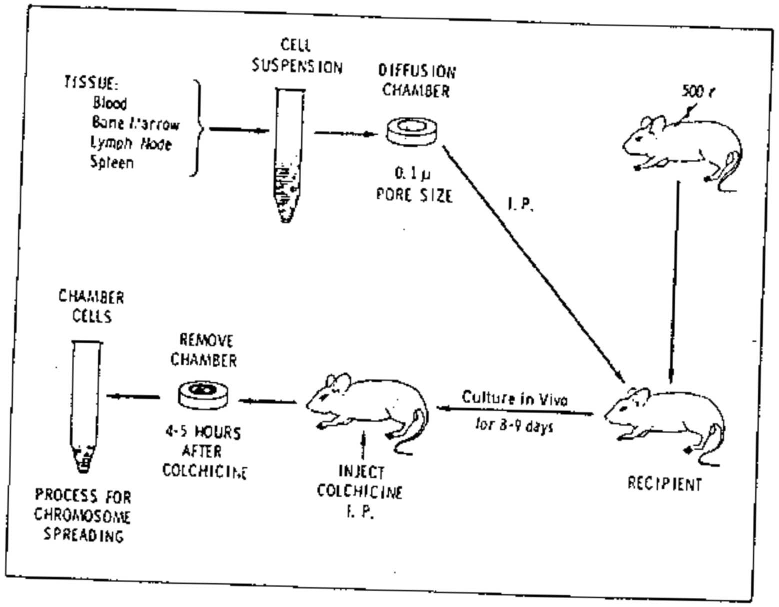


Diagram of a method to cultivate primate cells to obtain mitotic figures for cytogenetic analysis.

Immunologic Studies

It was demonstrated that human lymphnodal tissue can be successfully frozen and stored as viable cells. The freezing and storage effects on the viability have been assessed, with a significant finding that there is a delay in proliferation and cellular differentiation of cells during cultivation in diffusion cnambers correlated with the delay in the formation of antibody.

The cultivation studies with human lymph node tissues have continued, and a study was carried out to determine the proliferative capacity of the antibody-containing cells, as compared to cells in the same population that were not forming antibody. An immuno-histo chemical staining was performed using fluorescein conjugated antityphoid serum, and it was found that competent antibody-containing cells proliferated at a greater frequency than incompetent cells during early phases of antibody synthesis. The proliferative capacity is reduced to normal levels during the later phases of antibody synthesis. Frequency of tritium labeling in

antibody-containing cells increased on days 10 to 12 and was three to four times greater than the cells in the total cultured population. These data suggest that the mature antibody-containing cells are derived from immature precursor cells through somatic division.

A study was conducted to investigate the synthesis of two molecular forms of antibody. The study thus far indicates that the primary source of the 7S antibody protein in a mouse is in the spleen and that although the immune serum appears to contain predominantly this low molecular weight protein, cells capable of synthesizing 19S antibody were present in both lymph node cells and in the thymus. The data also confirm the thesis that thymus cells from pre-immunized animals have antibody-forming potential. Studies in progress indicate their ability also to initiate a primary response in diffusion chambers.

Experimental Studies on a Small South American Primate

The immunology program of the Division has continued to develop the use of the small monkeylike primate, *Tamarinus nigricollis*, for laboratory studies. It has been discovered that the animal is quite radiosensitive as compared with other primates and mammals, and the apparent radiation sensitivity does not extend to the immunologic activity. Animals showing a pronounced hematopoietic sensitivity, and bleeding to death, still have been able to produce antibody in response to stimulation.

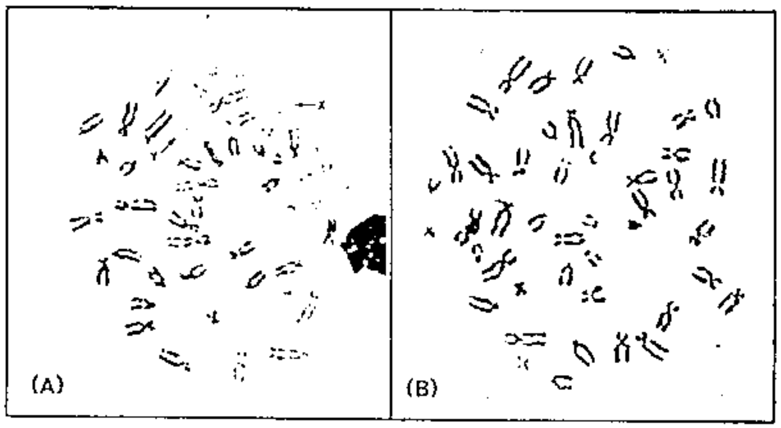
It has been discovered that natural chimerism exists in these animals by virtue of vascular anastomosis of the placenta during the intrauterine development. Evidence for male-female chimerism has been obtained by cytogenetic analysis for sex chromosomes. The use of the sex appendage on the granulocyte as a transplantation marker among tamarins would be limited, being applicable only to those situations where the absence of such cells in potential male recipients could be shown conclusively. The existence of the natural chimerism is an intriguing discovery and suggests that the animal may have unique attributes for the study of immunologic tolerance to donor tissues.

The mammalian cytogenetics program was initiated in August of 1963. Utilizing the peripheral blood technique, studies are being carried out on gamma-induced chromosome aberrations in patients receiving total-body irradiation therapy, blood from normal individuals irradiated *in vitro*, and monkey blood (South American spider monkey *Ateles*) irradiated both *in vitro* and *in vivo*. A comparison of the results, although still very meager, shows fairly good correlation both *in vivo* and *in vitro* and in monkey and human data.

Chromosome analysis of dividing peripheral blood cells of *Tamarinus nigricollis* is being done to determine chimerism and the per cent of chimerism in this animal. It has been found that an animal exhibiting a male-female chimerism contains this chimerism not only in the peripheral blood but in other hemapoietic tissue as well.

Medical Radionuclides and Metals Metabolism

Work continued on evaluation of factors affecting selective localization of radioactive materials after intralymphatic injection. Interest in this project is based on the need for radioactive isotopic methods for localizing and delineating lymph nodes and showing enlargements or replacements by tumor, and to evaluate the possibility of using radioactive isotopes for selectively delivering radiation to lymph nodes involved in a malignant process.



(A) Cytogenetic preparation of cultured blood cell. Mitotic figure of a male cell in a female tamarin (note Y chromosome) indicating intrauterine mixing of blood between male and female twin. (B) cell from male tamarin lacking Y chromosome indicating its female origin.

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Factors that have been considered have been particle size of colloids or microspheres and chelates of rare earths. Results emphasized the importance of both the size and the chemical composition of colloidal or suspended particles in determining lymphatic localization and circulatory distribution after lymphatic injection.

Studies have continued on the induction of acute fatty livers after intravenous doses of lanthanon chelates. Comparisons have been made in parallel studies of cerium, neodymium and samarium with complexes of chloride, citrate, HEIDA, NTA, NEDTA and EDTA. One mechanism to explain the metabolic impact of one of these agents manifested grossly as fatty liver would assume the blocking of an essential enzyme system. Since recovery regularly occurs, the assumption would be that the cellular source of this system is not killed but that only the existing supply of enzyme is blocked or bound irreversibly. Repeated experimental evidence shows the critical damage to occur at the time of the intravenous dose, while the prominent liver localization proceeds gradually over several hours.

Sephadex chromatography and disc electrophoresis are being evaluated as preparative and as analytical tools for study of the protein-metal binding postulated to explain rare earth fatty liver. Sephadex is a cross-linked dextran proposed for separations by gel filtration, and disc electrophoresis is done in polyacrylamide gel.

An interesting phenomenon has been discovered in the distribution patterns of cesium-137 and its daughter, barium-137m. Even though the half-life of the barium-137m is quite short, the distribution pattern differs significantly from that of its parent. The overage of barium-137m in the blood might conceivably be a useful index of some dynamic process. Attempts were made in rats to alter the circulation and the general metabolic rates by anesthesia, hypothermia, hyperthermia and stunning. Vasoconstrictors and vasodilators also have been tested. At present, it is thought that the percentage of barium-137 mobilized is possibly an indicator of the general metabolic rate.

Radioisotopes in Diagnosis and Therapy

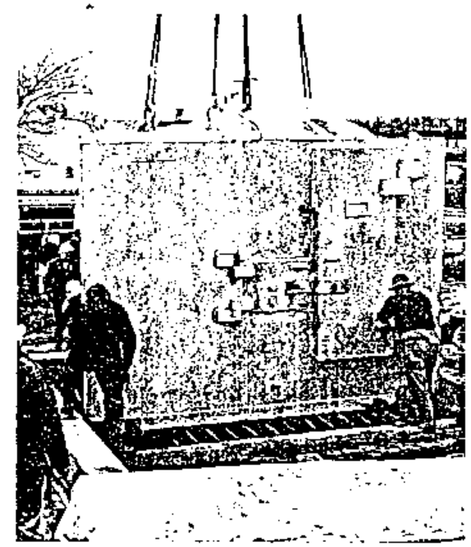
Attempts to measure blood clearances of radioactive test compounds usually have depended on multiple venipunctures from an arm or leg vein. With the availability of an arm counter which permits the measurement of the amount of radioactivity circulating through the arm, the Division has begun tests and evaluations of clearances of test agents from blood by this method. For example, it has been observed by others that plasma binding sites for vitamin B_{12} are abnormally abundant in persons with chronic myelogenous leukemia, and an intravenous injection of radioactive vitamin B_{12} leaves the blood at a slower than normal rate. Since as much as 1 per cent of the whole blood volume is present in the arm, it is possible to detect minute amounts of radioactive injected material by external arm counting. The arm is placed within the special liquid-scintillation-well counter, and radioactivity is charted following an intravenous injection into the other arm. This method shows that patients with chronic myelogenous leukemia clear the vitamin B_{12} from the arm much more slowly than do normal persons. Comparison of these curves with those from simultaneously obtained aliquots of blood reveal that the assays made with the arm counter include radioactivity from a compartment or space within the tissues of the arm outside of the peripheral vascular space. Studies suggest that there is altered diffusion of vitamin B_{12} in chronic myelogenous leukemia into these extravascular and interstitial spaces.

In another experiment with the arm counter, blood clearances of colloidal gold-198 indicated that only 70 per cent of the isotope disappeared with a half-time compatible with hepatic and bone marrow removal of the colloid. The other 30 per cent is retained in the tissues of the arm by some as yet unknown process.

Medical Instruments Development

The Division has continued to develop its whole-body counting instrumentation facility with the aim to cover a continuous patient-activity range from therapeutic doses down to natural body background. The required instrument-sensitivity range is more than 100,000,000 to 1. To encompass this range, three separate whole-body counting systems are required. The high-level counter has been constructed and is in clinical operation. The diagnostic-level instrument was developed during this past year and, after an initial calibration, has also been placed in operation. The low-level counting facility is nearing completion with the eight large scintillation crystals currently being installed.

The new diagnostic-level, whole-body counter is essentially an array of four 3" x 3" scintillation crystals mounted in a collimating



The low-background 60-ton steel box for the new low-level whole-body counting facility is set into place.

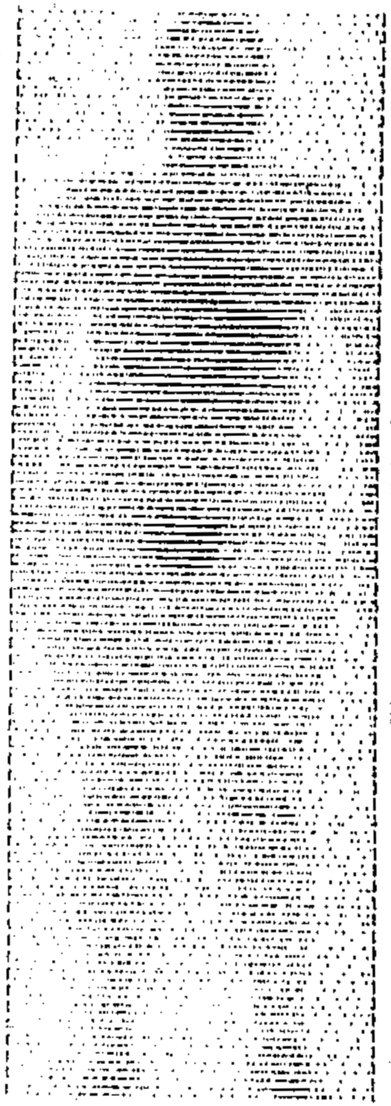
trough of lead. The trough is 1¼" thick and weighs 3,000 pounds. This troughlike collimator allows all the crystal detectors to view the entire patient, and all detected counts will be summed into one input for the spectrometer system. The subject reclines on a special X-ray stretcher which is radiolucent; the stretcher is then wheeled to the collimator-detector assembly where the counts are made.

Rigorous testing of the shielding and equipment for the new low-level, whole-body counting facility resulted in an extremely minimal background radiation level. A low-level, 60-ton steel box is being used in this counter. Two large hinged doors on the front of this box are for the introduction of patients into the low-background counting chamber, and also to allow maintenance personnel to enter for equipment adjustment.

A new whole-body scanner has been designed and constructed in collaboration with Oak Ridge National Laboratory; it employs a 4" x 5" scintillation crystal and a highly efficient, 84-hole lead-focusing collimator. The remote recording system uses a 5 to 1 reduction ratio, so that a 60" patient produces a 12" record. An additional photorecording system is under construction. With this instrument it is possible, with suitable doses of radioactivity, to obtain a whole-body scan of a patient within approximately one hour. At this scanning speed, however, fairly large doses of radioactivity have been required. Initially, the two main uses for this instrument were detecting metastatic thyroid carcinoma and mapping out the localization of the hematopoietically active bone marrow.

Additional instrument development activities included design and construction of a plexiglass arm phantom containing many compartments for the arm counter program and development of a two-headed, large-volume, radioactive sample counter designed to measure accurately the radioactivity in bulky samples for variable sizes and shapes without the necessity for corrections for spatial distribution of radioisotope in the sample. Such an assay system was needed, particularly for quantitating iodine-131 in total 24-hour fecal specimens. The design consists essentially of two vertically opposed, 2" x 2" sodium iodide crystal detectors placed 24.75" apart, viewing a chamber shielded with 4" of lead.

Another activity in the instrumentation development consisted of a three-dimensional, integral analysis using isoresponse data to evaluate collimation for external counting of chromium-51 in the spleen. In certain types of hemolytic anemia the red cells are sequestered by the spleen, and this can be demonstrated by the increase of radioactivity in the spleen after an intravenous injection of red cells labeled with chromium-51. It has been difficult to quantitate the accumulation of activity by external detectors, and this study was aimed at the evaluation of lead collimators used for spleen counting.

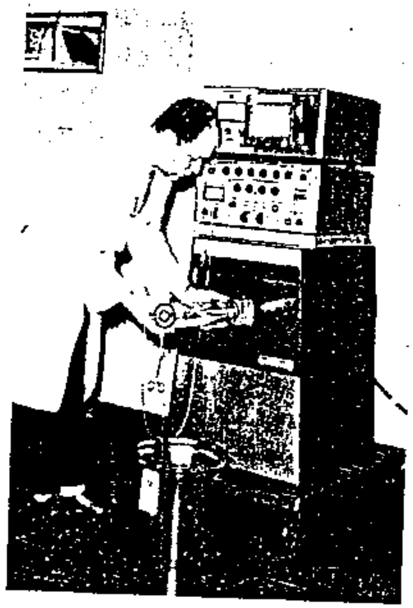


The two main uses of the new whole-body scanner during the year were detecting metastatic thyroid carcinoma and mapping out the localization of the hematopoietically active bone marrow.

Clinical Scanning

The Division continued to work on problems of describing the size and location of the blood-forming organ, the bone marrow. Heretofore, this organ has been difficult to locate and quantitate. The areas of active blood formation vary from person to person, depending on age, responses to infection, or to diseases involving the bone marrow. Radioisotope scanning techniques have been shown to provide considerable assistance in determining the size and distribution of the organ. The Division has been able to clearly delineate the bone marrow using intravenous colloidal gold-198. Nearly 60 patients with a variety of disorders of blood cell formation have been studied with this technique, using both area scanning and linear scanning. Linear scans usually give some quantitative estimation of the distribution of marrow along the trunk and are useful in showing abnormal extensions of the marrow outside of the trunk. In addition, contraction or regional destruction of the marrow outside of the liver peak can be measured quantitatively. Thus a broader, more comprehensive view of the blood-forming organ can be obtained. Because of the relatively large doses of colloidal gold-198 now required, other tracer isotopes are being investigated. Since the use of colloids for bone marrow scanning is premised on a close correlation of blood cell function and reticulo-endothelial function in red marrow, other radiocolloidal preparations promise to have advantages in terms of shorter half-life or more suitable gamma energies. Therefore, an animal study has been begun to test a variety of colloids. Technetium-99m, in theory, is an attractive new isotope. It is obtained by elution from the parent molybdenum-99m generator. This isotope has a 140 kev gamma emission, a six-hour physical half-life, and no beta emission. Sulfur sol preparations have not, until now, been satisfactory, and the preparation of a uniform, small-particle colloid of this isotope remains as an unsolved problem. Chelates of selected rare earths may be feasible and may produce compounds with suitable characteristics, and pilot studies have begun.

The scanning program also has been devoted to evaluation of scanning of subarachnoid spaces after intrathecal injection of



Instrument development activities included design and construction of a plexiglass arm phantom.

iodine-131 albumin. Although this procedure was suggested a number of years ago, the earlier scanning equipment was inadequate. With the availability of the Oak Ridge National Laboratory research scanner, reassessment of the procedure was carried out, and it has been possible to demonstrate complete compression of the spinal cord. The material spreads along nerve root sheaths. In one instance it was possible to show a unilateral impaired spread correlating with the clinical symptoms of epidural infiltrations. At 24 hours in one patient, focal activity in the site suggested retained radioactivity at the site of the tumor. The simplicity of the procedure offers some theoretical advantages over conventional contrast media injections for X-ray.

AEC-NIH Ultracentrifuge Development Program

In a preliminary pilot study at Oak Ridge National Laboratory, using differential and zonal ultracentrifugation of samples of plasma from eight leukemic patients at the Division, viruslike particles were discovered in electron-microscopic examinations. Two morphologically different (Q,R) particles were observed in these patients, while 18 controls contained no particles of the R

variety, but one Q-like particle. Subsequently, a collaborative collection effort was begun with the cooperation of some of the member institutions of the Oak Ridge Institute of Nuclear Studies. At the time of this report, more than 300 samples of plasma from patients with leukemia, lymphoma, or multiple myeloma had been received; ultracentrifugation concentrations followed by electron-microscopic scannings are in process. The cooperating institutions have supplied, in addition to the plasma samples, selected information concerning the patients' histories, and this information is being coded on IBM cards so that a variety of correlations can be made with the electron-microscopic and centrifuge results. The recent advances in animal cancer and leukemia research strongly indicate implication of a virus, and, therefore, this effort is regarded as a significant attempt to isolate and identify particles which may be related to leukemia.

Retrospective Study on Radiation Effects in Man for NASA

The Division has been requested to make a retrospective study on the available data of radiation effects in man, assembled and analyzed in such fashion as to be useful to the National Aeronautics and Space Administration in anticipating radiobiologic problems in manned space flights. The purposes of this study are to bring together all available information of potential use in evaluating the problem of irradiation of man in space flight, to correlate radiation effects with dose, to predict the probability of radiation effects, and to extrapolate these results and probabilities to fit expected conditions in space. The immediate objective is to study the effects of total-body gamma irradiation upon the well-being and clinical course of 88 patients who have been treated with total-body irradiation at the Division.

A method for extracting data from clinical histories into an alpha-numeric translated form that can be used in computer processing has been developed for those portions of the chart concerned with symptomatology, observations by the nursing and medical staffs, biochemistry, hematology, drug therapy and radiation dosimetry. For the needs of NASA, this retrospective study will have the following features: (1) incorporation, insofar as possible, of all data that may have biological importance on the effects of radiation in man, (2) open-ended data compilation for addition of new cases as they become available, and (3) systematic use of data retrieval and computer techniques which will allow rapid extraction, analysis and correlation of all available information so that reevaluation and new correlations can be made as the need becomes apparent.

Training

The Division encouraged staff members to take advantage of specialized training opportunities. Two staff members attended a Tri-Carb school and one completed a training conference on the analysis of chromatograms.

In addition, the Division offered a variety of training experiences to scientists from a number of foreign countries. There were visitors from Germany, the Philippines, Japan, India, Turkey, Thailand and Korea. There were five Abbott fellowship medical students, five short-term residents from Massachusetts General Hospital and one from Memphis Methodist Hospital, and eight trainees from the Summer Student Trainee program at the Division.

Members of the staff work on data collection from clinical records for the National Aeronautics and Space Administration study on human radiation effects.

The Division assisted the Special Training Division in its program to provide qualification courses for physicians in radioisotope handling. Clinical aspects of the courses were given at the Division and staff members provided lectures and clinical demonstrations.

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Special Symposium

From October 21 to October 25, the Division conducted a symposium on Dynamic Clinical Studies with Radioisotopes. Co-chairmen for the symposium were Ralph M. Kniseley of the Division, and W. Newlon Tauxe of the Mayo Clinic. Two hundred and three participants attended the meeting, and 35 speakers participated, including C. C. Lushbaugh of the Division staff, and C. Craig Harris, of Oak Ridge National Laboratory. Among the foreign speakers were: Erik E. Bergner, Karolinska Institutet, Stockholm, Sweden; Cesare Fieschi, University of Genoa; Sheila Sherlock, Royal Free Hospital, London; A. S. McFarlane, National Institute for Medical Research, London; L. Donato, University of Pisa; Eric Pochin, University College Hospital Medical School, London; David C. Price, Toronto General Hospital; John B. West, Postgraduate Medical School, London; and David V. Bates, McGill University, Montreal.

The proceedings of the symposium were published in June 1964.

Visiting scientists and a member of the Medical Division staff operate a multichannel analyzer for taking gamma ray spectra in the whole-body counter.

TRAINEES IN CLINICAL INVESTIGATION

Peter Pfannenstiel—Rotenberg, Germany
Pureza Flor Gaerlan—Cavite, Philippines

JAMES PICKER FOUNDATION FELLOWS

Takashi Honda—Kanazawa City, Japan
Guio Uchiyama—Tokyo, Japan

ABBOTT STUDENT FELLOWSHIPS IN NUCLEAR MEDICINE

Arthur E. Diamond—Tulane Medical School, New Orleans, La.
Sheila Hodgson—Woman's Medical College of Pennsylvania
William E. Rhodes—Meharry Medical College, Nashville, Tenn.
Carl E. Drake—Meharry Medical College, Nashville, Tenn.
Vernon Kraus—University of Cincinnati

RESIDENT PHYSICIANS

Richard J. Steckel—Massachusetts General Hospital, Boston
Roland J. Ware—Massachusetts General Hospital, Boston
Donald L. Stone—Massachusetts General Hospital, Boston
William J. Otto—Massachusetts General Hospital, Boston
Luiz F. Mattoso—Massachusetts General Hospital, Boston
James E. Hancock—Methodist Hospital, Memphis, Tenn.

VISITING SCIENTIFIC GUESTS

J. P. Goyal—India, International Atomic Energy Agency Fellowship

Orhan Ternar—Turkey, International Atomic Energy Agency Fellowship

Makumkrong Wasanosomsithi—Thailand, International Atomic Energy Agency Fellowship

Pedro N. Mendoza—Philippines, International Atomic Energy Agency Fellowship

Young Ja Lee—Korea, International Atomic Energy Agency Fellowship

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MEDICAL DIVISION CLINICAL CONFERENCES—1963

July 11: Proliferative activity of antibody-forming cells — Paul Urso, Seton Hall University, South Orange, N. J.

July 18: Meeting report, Society of Nuclear Medicine, Montreal, Canada—Medical Division staff members.

July 25: Binding of Cr^{51} to hemoglobin — Howard A. Pearson, Department of Pediatric Hematology, University of Florida College of Medicine, Gainesville.

August 1: Spleen scanning with Cr^{51} labeled red cells — Guido Luzzatti, Instituto di Radiologia, Instituti Ospitalieri di Milano, Italy.

August 8: Demonstration of IBM card-handling equipment—A. L. Kretchmar.

August 15: Work report: summer college trainees on (a) medium-level whole-body counter design, (b) resin uptake of triiodothyronine, (c) radiation safety—John Brucer, Maxine Schwartz, Paul Wills.

August 22: The nutria as a laboratory animal—Everett D. Wilson, Sam Houston State Teachers College, Huntsville, Tex.

August 29: Synthesis of alkenyl ethers of glycerol — Claude Piantidosi, University of North Carolina, Chapel Hill; Synthesis of C^{14} alkoxyglycerols—Paul Godfrey, Louisiana State College, Pineville.

September 5: Experience with data processing devices in hospital management—J. Howard Harmon.

September 12: Human cytogenetics program at Children's Hospital, Winnipeg, Canada — John Melnyk, Staff Cytogeneticist, Children's Hospital, Winnipeg.

September 19: Comparison of collimation of gamma-ray detectors: a 3-D integral analysis of isoresponse data, with application to external counting of Cr^{51} in the spleen—Bill M. Nelson.

September 26: Modified runge-kutta method for the solution of sets of linear and nonlinear differential equations with the digital computer—J. D. Lawson, Lecturer in Mathematics, Department of Mathematics, University of Waterloo, Canada.

October 3: Data collection, patient monitoring, and medical research computing — Don R. Williams, IBM Data Processing representative, IBM Data Processing Division, Knoxville, Tenn., and Wolf Helmerick, IBM representative, New York City.

October 10: The significance of plasma of amino acid levels — Marian Swendseid, School of Public Health, University of California, Los Angeles.

October 17: Isolation of viruses from tissues in the zonal centrifuge—N. G. Anderson, Biology Division, Oak Ridge National Laboratory.

October 31: A yeast mitogenic factor active on human peripheral leukocytes—Enrico Gandini, Department of Medical Genetics, University of Washington School of Medicine, Seattle.

November 7: Analog computer model of rose bengal liver function test—A. L. Kretchmar.

November 14: Fatty acid synthesis in the lactating mammary gland—John Coniglio, Department of Biochemistry, Vanderbilt University School of Medicine, Nashville, Tenn.

November 21: Tests of parathyroid function—Herschel L. Estep, Department of Medicine, Medical College Hospital, Richmond, Va.

December 5: Computer applications—A. L. Kretchmar.

MEDICAL DIVISION CLINICAL CONFERENCES—1964

January 9: Speculation on the probable effects of irradiation on the lipid molecule and the subsequent metabolic consequences —James N. Bollinger.

January 16: Present status of whole-body counting program — Members of the staff.

January 23: Bone-marrow scanning project—Ralph M. Kniseley.

January 30: Technetium-99m scanning in rats: an introductory study—Granvil C. Kyker.

February 6: Hemoglobin A_4, a hemoglobin tetramer found in normal blood—Amoz Chernoff, University of Tennessee Memorial Research Hospital, Knoxville.

February 13: Design of experiments from a biostatistician's point of view—Raymond Roth.

February 20: Iron turnover in tumor-bearing rats—F. Comas.

February 27: Discussion of homotransplantation conference in New York and irradiation facilities available at ORINS — N. Gengozian and Roger Cloutier.

March 5: Hemolytic anemia secondary to macroglobulinemia, clinico-pathologic conference — C. W. Sensenbach, Oak Ridge, Tenn.; W. J. Otto, Bill M. Nelson, and N. Gengozian.

March 12: Some problems of radiation in space—Wright Langham, Director of Biomedical Research Group, Health Division, Los Alamos Scientific Laboratory, Los Alamos, N. M.

March 19: Report of symposium concerned with biomedical research and clinical application of I^{125}, Chicago, February 1, 1964—William D. Gibbs.

March 26: Working conference—A. L. Kretchmar.

April 9: Can a human cell partially depleted of DNA still multiply?—Robert S. Chang, Harvard University School of Public Health.

April 16: Low-level whole-body counter: construction report and preliminary background radioactivity results—A. C. Morris, Jr.

April 23: A compartmental interpretation of yttrium distribution —Bergene Kawin, Assistant Chief, Radioisotope Laboratory, Veterans Administration Hospital, Fort Howard, Md.

April 30: Zonal scanning of thin-layer chromatograms as related to lipid metabolic studies—Fred Snyder.

May 7: *In vivo* mobilization of barium-137m—Raymond L. Hayes.

May 14: Highlights of I.A.E.A. scanning symposium in Athens, Greece—Ralph M. Kniseley.

May 21: Bone marrow scanning studies on animals—Granvil C. Kyker.

May 28: Infections in patients given total-body irradiation—G. A. Andrews, B. M. Nelson, and B. W. Sitterson.

June 4: Natural chimerism in tamarins—N. Gengozian.

June 11: Irradiation under anoxia of a carcinoma of the gingiva— F. Comas.

June 18: Research programs at the Special Training Division of ORINS—Lawrence K. Akers, Special Training Division.

June 25: Patterns of DNA replication in the mammalian chromosome complement—Anil K. Sinha. Department of Genetics, McGill University, Montreal, Canada.

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**On leave of absence to International Atomic Energy Agency*

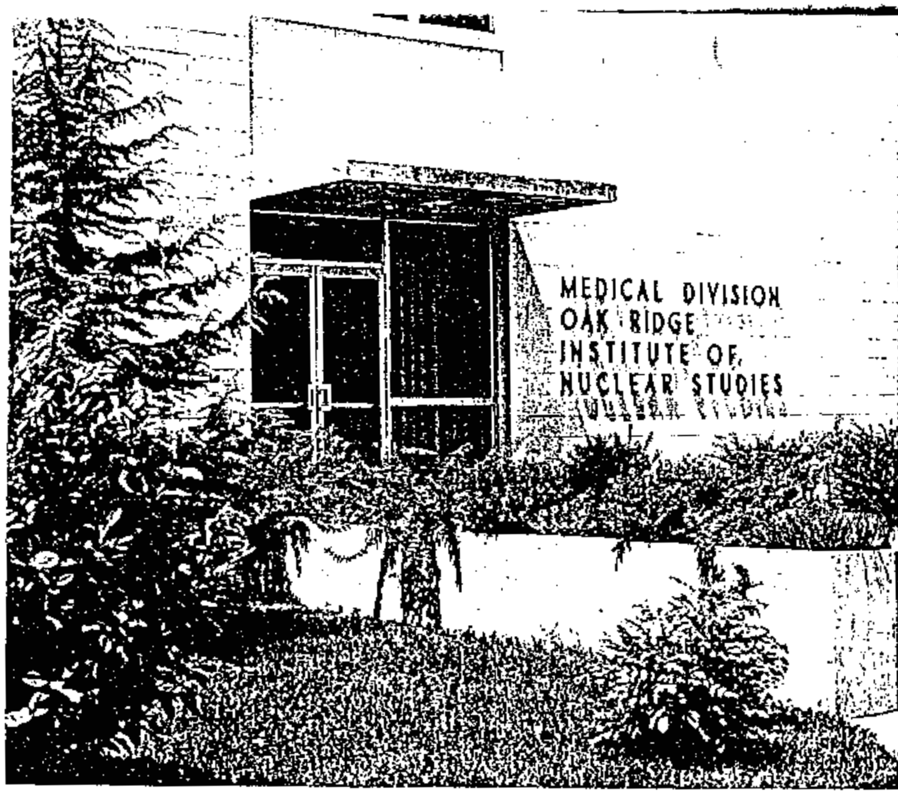
6/30/65

Oak Ridge Institute of Nuclear Studies

Nineteenth Annual Report

OPERATING UNDER CONTRACT WITH
UNITED STATES ATOMIC ENERGY COMMISSION

JUNE 30, 1965



Medical Division

The Division of Biology and Medicine of the U. S. Atomic Energy Commission, as a part of a large biomedical program, supports a small group of "on-site" projects that have clinical research facilities. The Medical Division of the Institute is one of these.

The Medical Division operates a 34-bed research hospital for its clinical research, and also has laboratories in the clinical and basic sciences. During the last year the program has continued to grow, with three additions to the senior staff. C. Lowell Edwards, Chief of the Clinical Services, formerly with the U. S. Public Health Service Hospital, Staten Island, N. Y., replaced Beecher Sitterson who resigned to take another position. Kong-oo Goh, previously with the University of Rochester, assumed responsibility for the cytogenetics program, and Virginia Holten, who re-

cently completed her training at the University of North Dakota, joined the metals metabolism group.

Among the noteworthy events of the year were completion of the low-background whole-body counter, the initiation of the testing and clinical program with this facility, and the start of the cytogenetics program in full.

Papers on a variety of topics were presented at regional and national meetings, and the Division also was represented at international meetings. Fred Snyder presented a paper on *Zonal Thin-Layer Chromatography* at the Symposium on Radioisotope Sample Measurement Techniques sponsored by the International Atomic Energy Agency in Vienna. Gould A. Andrews, Division Chairman, presented an invited paper at a conference on radiation accidents and protection in Vienna. Arthur Kretchmar presented a paper at a conference on bone-marrow transplantation in Paris.

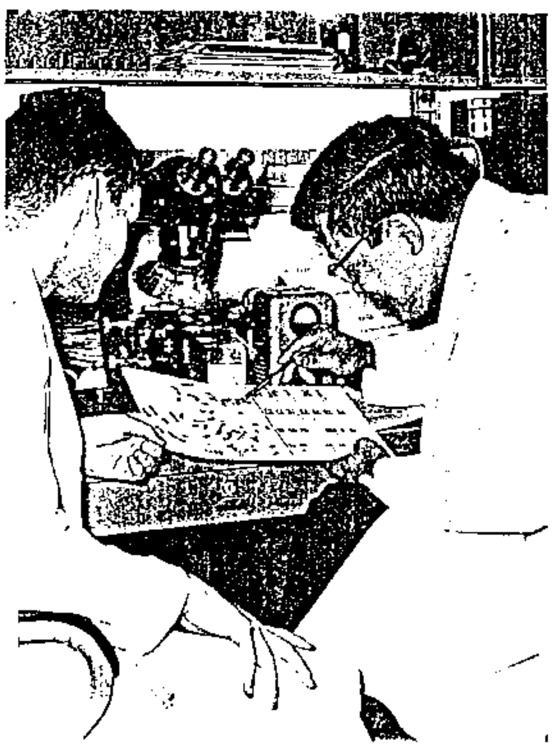
As a part of increased communications with laboratories outside Oak Ridge, two staff members were assigned to other centers for extended periods of collaborative work. Frank Comas, radiotherapist, is spending nine months in the laboratory of Henry Kaplan at Stanford University. Fred Snyder worked for five months with Claude Piantadosi, synthesizing labeled compounds at the University of North Carolina.

A new program was initiated with the department of biochemistry at the University of Tennessee Medical School in Memphis, through the cooperation of John L. Wood, chairman of the department. Two Institute staff members were given faculty appointments in the Medical School. Each presented a series of lectures at Memphis, and further collaboration was developed, one aspect of which involved use of the Institute's analog computer. As part of this activity, a plan was organized for a joint graduate student program leading to an advanced degree.

Mechanisms of Radiation Injury and Treatment

This is a major, broad objective of the Division program, and includes elucidation of certain mechanisms of damage, both acute and subacute, with emphasis on those effects characterized by hematologic, biochemical, immunologic and cytogenetic changes. Analysis of the approximately 100 patients who have been treated in the total-body irradiation program has included a study of the infections that occur after exposure. In the high-dose group (200 to 940 R body air dose), a variety of serious infections has been encountered, ranging from superficial skin infections with *Staphylococcus aureus* to fatal systemic infections, sometimes by organisms not usually pathogenic. The prominence of gram-negative infections and fungi was emphasized in this series, and its appears that leukopenia is the major feature in the susceptibility to infection. The responses of cellular components of the blood to various doses of radiation have been studied, emphasizing the changes caused by lower doses (50 and 100 R) in patients with chronic neoplastic diseases, particularly chronic leukemia and lymphosarcoma.

The program in lipid metabolism and irradiation has been concerned principally with changes in the bone marrow, since it has been observed that the amount of fatty tissue in the marrow increases after irradiation concurrently with the disappearance of the blood-forming cells. Research has revealed, for example, that the fatty change occurs in the bone marrow only in sites directly exposed to ionizing radiation, and it has been shown that irradiation stimulates locally the biosynthesis of triglycerides in non-



A staff scientist and trainee analyze a chromosome preparation in the cytogenetics research project.

fatty stem cells of the marrow. The great increase in fat irradiated bone marrow appears to be primarily caused by t stimulation of the biosynthesis of fatty acid esters and, to a les degree, by the inhibition of the oxidation of fatty acid. By administration of radioactive-labeled fatty acids to animals gi total-body irradiation, a significant increase in the total amou of radioactivity in the bone marrow has been detected, mos present as fatty acid esters in the triglyceride fraction. Additio work has included the study of the effects of dietary fat and tot body irradiation on the fatty acid composition of bone marr lipids. Neither the amount of fat in the diet nor the type of (saturated vs. unsaturated) had an effect on the total amount fat accumulated in the bone marrow of rats exposed to total-bo irradiation. On the other hand, the fatty acid composition of t dietary triglycerides influenced qualitatively the fatty acid co position of the irradiated marrow.

An interesting phenomenon related to the exposure rate which total-body irradiation is given to animals has been disc ered in the immunology program. Mice given 900 R of total-bo irradiation at varying exposure rates differed significantly in th ability to accept grafts of rat bone marrow. Only a temporary ta occurred in those exposed at a low rate (3.7 or 19.8 R/mi Permanent grafts were obtained only in those treated at hi exposure (39.7 and 53 R/min). Early active antibody formati against rat erythrocytes appeared after disappearance of the gr in the group treated at lower exposure rates.

Animals exposed to total-body irradiation can be saved fr death by donations of marrow from healthy donors. If the don is not of the identical strain, many of the animals develop a serio disease, which is not a direct result of the irradiation, but a resu of the immunologic effects of the engrafted marrow. Studies the Division, carried on in collaboration with the biology divisi of Oak Ridge National Laboratory, and with Knoxville Colleg have made important progress in clarifying this so-called seconda or homologous disease.

The disease is approached as a general metabolic disord Early changes are seen in the levels of aspartic acid in the liv and of muramidase (lysozyme) in the kidney. These change coming before the obvious manifestations of secondary disease a pear, indicate a profound injury to the host metabolism caused l the donor marrow. One aspect of the secondary disease picture loss of weight without a negative nitrogen balance. This indicated an important redistribution of nitrogen in the host. On the basis of these studies, it has been suggested that some of the nitrogen is shifted to extracellular antigen-antibody complexes. Preliminary information suggests that a significant portion of the excess nitrogen may be in the skin, an organ that shows profound changes in secondary disease.

These studies have great importance because of the growing clinical use of tissue graft procedures.

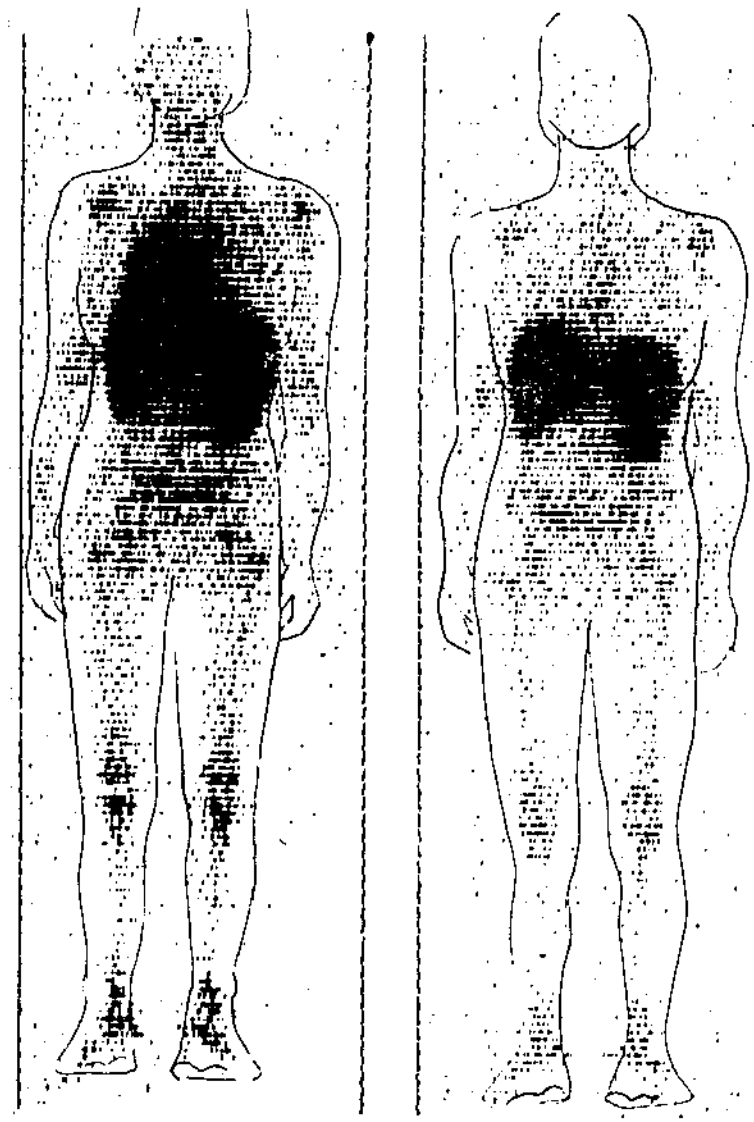
Experimental Studies on a Small South American Primate

The Division has continued its program in the development of the *Tamarinus nigricollis* primate as a laboratory animal for special radiobiological and immunologic studies. Bone-marrow grafting attempts after total-body irradiation have demonstrated the efficacy of marrow cells in prolonging survival, but the results substantiate further the reports of others on the difficulties of obtaining therapeutic homologous grafts in irradiated primates. The failure of the homologous marrow to extend the survival times of animals receiving 400 R suggests that this was due to an active immunologic rejection of the graft by the host.

Related studies have extended the information previously discovered concerning the natural chimerism that occurs regularly in the marmoset. This is the survival of hematopoietic tissue exchanged *in utero* from a nonidentical twin, a finding that offers unique opportunities of tolerance. Support for these studies has been granted by the National Institutes of Health. Recently, this program has achieved pronounced improvement in the health of the animals and successful breeding of several pairs.

Metals Metabolism and Medical Radioisotope Development

An important objective is the development of new isotopic labels and compounds that may have clinical application. A series of hematopoietic marrow scans was performed on animals that received preparations of rare-earth citrates of varying pH; the uptake in marrow is based on reticuloendothelial cells associated with hematopoietic elements present. A promising compound was developed, ^{159}Gd hydroxycitrate, which was found to behave like a colloid at an acid pH, and has a convenient gamma energy and a short half-life. It is estimated that the radiation exposure to



Scans of a 44-year-old woman with acute granulocytic leukemia. The sca at the left was taken 3½ hours after intravenous administration of ^{159}G hydroxycitrate and shows less activity on the left side where she had a pleura effusion. The scan on the right, taken at 21 hours, shows sharper delineatio of the bone marrow, which has expanded into the lower extremities.

patients using this compound would be only about one-third of that from colloidal ^{198}Au when given intravenously for scanning the marrow. Another promising development from this group was the observation that ^{68}Ga, when prepared with suitable levels of carrier gallium in citrate form, localizes in bone. Gallium-68 is prepared from a ^{68}Ge generator, and has the advantage of the long-lived parent (280 days) and a short-lived diagnostic agent (T ½ = 68 min). Excellent detail has been observed in the skeleton of animals, and initial human trials have also been promising.

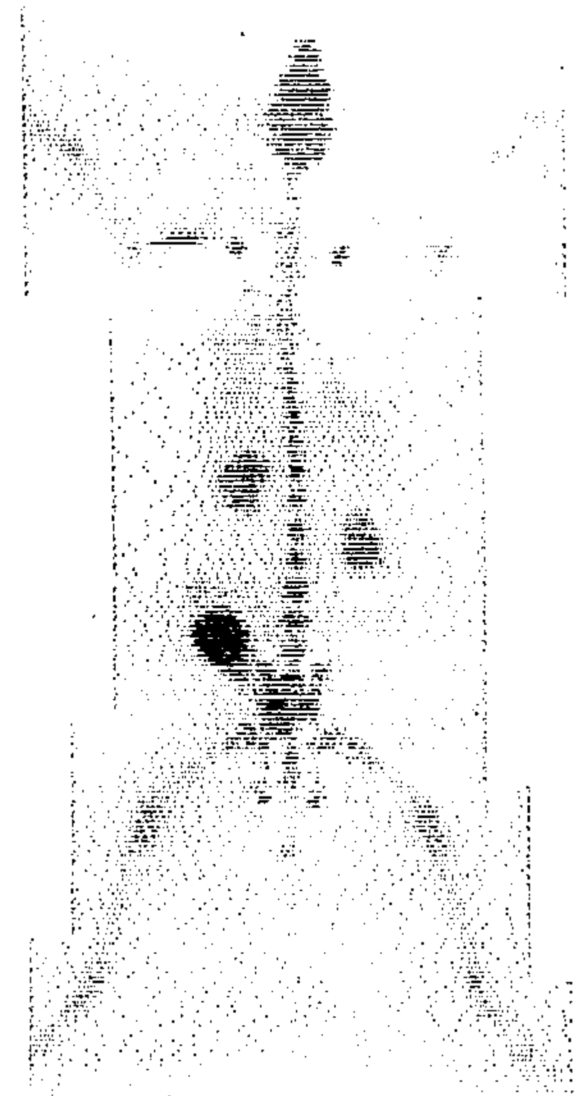
Work has continued on the elucidation of biochemical mechanisms related to the induction of acute fatty livers after intravenous doses of lanthanon chelates. An elevation of plasmalogens in the liver is one change that has been discovered, and in this particular experiment the results give the first indication of differences in the types of fatty livers caused by different elements in the cerium group of lanthanons.

Therapy with Radiation

The Institute's clinical program is focused mainly on problems relating to radiation effects in the human being, but there is also considerable work on diagnostic applications of radioisotopes, particularly in relation to malignant disease.

The studies of radiation effects are intimately tied with efforts to improve the treatment of disease in patients. These efforts include an intensive study of total-body irradiation in chronic leukemia, polycythemia, and some other hematologic and related disorders. External irradiation to local ports is also used, with some experimental approaches suggested by results in animal studies. Techniques for localizing disease are explored to treat more effectively cancer with irradiation.

During the last year a special study was done employing ^{130}I for diagnostic purposes in patients with cancer of the thyroid. This isotope, with its short half-life (12½ hr), makes possible repeated tracer studies in the same patient with a very low radiation dose and eliminates the difficulty with residual activity from previous doses, a problem that is encountered when ^{131}I, with its much longer half-life, is used. The ^{130}I was used to measure the effects of thyroid-stimulating hormone on patients with thyroid cancer. In five of 11 patients, whole-body retention of ^{130}I increased after the stimulating hormone was given, and three definite areas of ^{130}I, which had not been discernible previously, were seen in the



Gallium-68 citrate scan of a rabbit two hours after intravenous administration. The dose contained 5 milligrams of stable gallium per kilogram. The skeleton, kidneys and urinary bladder are clearly defined. The area of apparent deposition in the left arm is an artifact caused by leakage from the site of injection.

neck after TSH. Furthermore, in some patients the TSH enhanced the general whole-body retention of the radioiodine in a fashion not related to increased functional activity of normal or malignant thyroid tissue.

Conceptual design for a low-dose-rate whole-body irradiator was completed. This unit will provide a room large enough to permit continuous irradiation of patients at doses of 1 to 5 R/hr for periods up to two weeks. The contemplated study will attempt to answer the question concerning whether greater palliation can be achieved in certain chronic leukemias or lymphomas because of differences in repair rates between normal and neoplastic tissues at the low exposure rates. There will be 10 cobalt sources arranged geometrically to provide a uniform radiation field (within 10%) in the 14- x 14-ft. living space.

Radioisotopes in Diagnosis

The Division is working to use radioisotopes in diagnosis, to detect tumors, and to evaluate the size, location, and function of tumors already known to be present. Studies of functional or metabolic disorders, not necessarily associated with malignancies, are done with radioisotope tracers and unique counting facilities.

An intensive effort has been made in several research institutions to develop a diagnostic test for cancer of the bone. Diagnostic X-ray has been the mainstay of the clinician, but X-rays do not show an area of cancer until change in the bone structure is fairly extensive. Several radioisotopes are known to concentrate in areas of active bone damage, including those caused by cancer. Even in diseases that produce bone destruction, without X-ray evidence of new bone formation, active processes at the edges of the lesions are associated with increased deposition of certain of these radioisotopes.

In spite of the obvious need for a diagnostic isotope, the various ones tried all had disadvantages, either in availability, cost, or physical characteristics. Among these are ^{47}Ca, ^{18}Fl, ^{85}Sr, and ^{87m}Sr.

The Division is developing ^{68}Ga for this purpose. Gallium-68 is an isotope of short half-life (68 min) obtained from an isotope generator containing ^{68}Ge (half-life 280 days). When injected into an animal or a patient, ^{68}Ga localizes rather promptly in bone,

with the greatest concentrations in areas of growing bone or bone disturbance. There is also a significant amount in the kidney and, as a result of this kidney excretion, there is some in the bladder. The amount of carrier added appears to be important in determining localization, and this is also a subject previously studied. During the last year, excellent scans of experimental animals were made showing the skeleton with great detail and clarity. Clinical studies are currently under way.

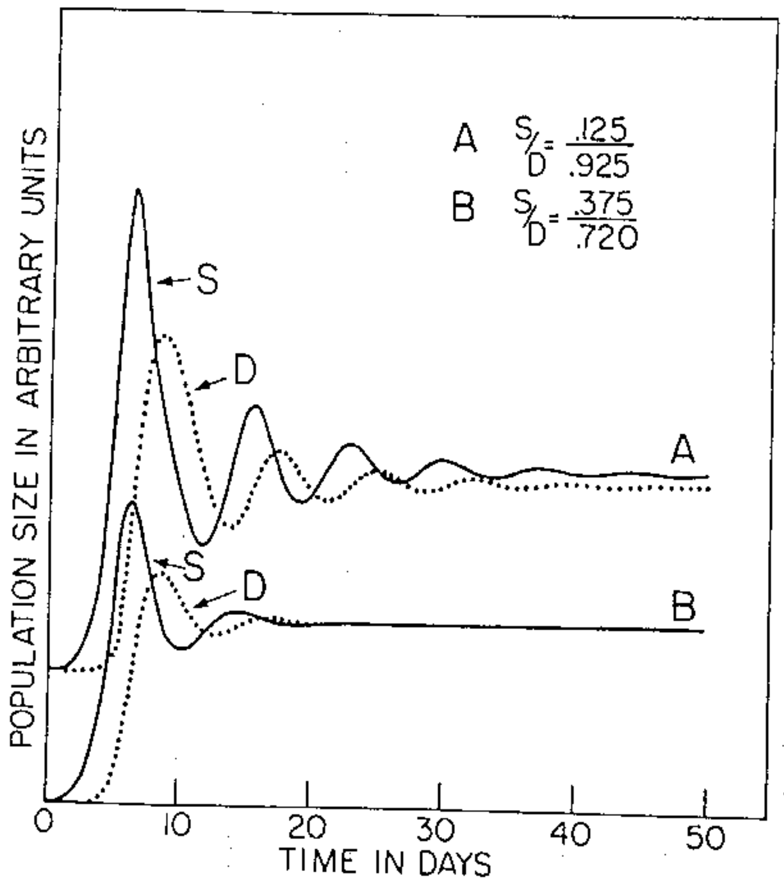
Scanning of the hematopoietic bone marrow in patients has been further advanced with the use of intravenous radioactive colloids. Although the earlier work was done almost entirely with colloidal ^{198}Au, more recent studies have used ^{159}Gd and ^{99m}Tc. Both isotopes have a shorter half-life and give less total-body irradiation than ^{198}Au. They are given in colloidal form so that the reticuloendothelial system takes them up. There is a considerable deposition in liver and spleen, and this is a disadvantage for the purposes of bone-marrow scanning.

However, it has been possible to show clearly the areas of functional bone marrow, and to make advances in clinical diagnosis. For example, the condition of myelofibrosis, in which the bone marrow is partially or completely replaced by fibrous tissue, is very easily diagnosed by marrow scanning. Certain local lesions, such as tumors in the bone marrow, or areas of radiation marrow damage, also are easily seen. A general observation has been that the expansion or contraction of the marrow with disease does not necessarily follow the clinical expectations, and the scans sometimes show rather remarkable variations from what might be anticipated if one assumes that the marrow alters its size in a predictable fashion to meet the need for hematopoiesis.

The whole-body scanner described in last year's report has been used rather extensively for this problem of marrow scanning. It allows a complete survey of the bone marrow in a single record and the scanning procedure is less time-consuming than that involved in multiple partial body scans. The study of bone-marrow scans is only beginning and it seems likely that in the future, with improved radioisotopes and improved scanning instruments, it will be possible to obtain excellent scans with very low radiation doses to the patient. With further clinical experience it should be possible to derive much more information from these scans, and they may become useful, not only in making diagnosis, but in following the course of hematologic disorders. They may also become an important part of the general survey for neoplastic metastases.

Systems-Biology

This program deals with several aspects of theoretical and mathematical biology. One of the major efforts is to set up models



An analog computer model of the stability and response of the red blood cell system. The ratio S/D is a measure of the relative competition between stem cells (S) and dividing erythroid (D) cells. In curves A, the S and D cells compete equally; in curves B, competition between cells of the same population (S cells) is greater than with cells of the other population (D cells). This kind of analysis may be helpful in understanding recovery after irradiation.

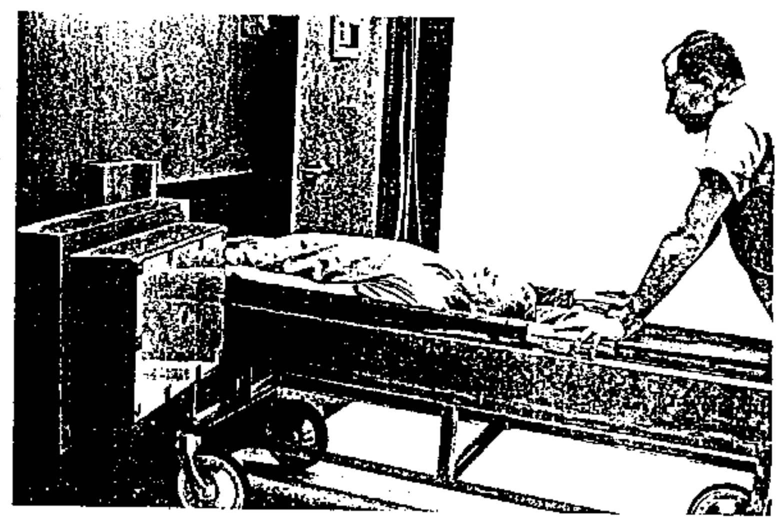
for certain cellular or metabolic systems that can be studied by means of the analog computer.

One of these is a model of the red blood-cell system. On the basis of known information about the amount of red cell forming tissue in the body, the time phases in the various stages of development of the red cells, and the survival and death of each cell type, a hypothetical model has been set up. The model is programmed for the analog computer in such a way that various assumptions about cell maturation and death can be simulated, and the consequences can be observed in the behavior of the analog system. This kind of analysis may be helpful in understanding the recovery of hematopoiesis after irradiation.

Another related study concerns the mathematical interpretation of data on red cell survival obtained from labeling techniques with materials such as $DF^{32}P$. Emphasis has been placed on the destruction rate rather than the average survival, and apparently improved clinical interpretation may be made from laboratory data.

Detecting and Localizing Radioactivity in Patients

The low-level, whole-body counting facility was completed, and put in operation, and during the latter part of the year a large



A side view of a subject being placed in the "cave" of the low-level whole-body counter.

number of normal persons and patients were surveyed in the instrument. Extensive standardization studies were done. Certain improvements were made to lower the background still further, and the instrument now appears to be almost ideal in its combination of a great sensitivity and very low background. A special advantage is the arrangement of the crystals so that the measurements made are almost independent of the location of the radioactive material in the patient. This is an advantage of a counter with multiple crystals over those that use one large crystal.

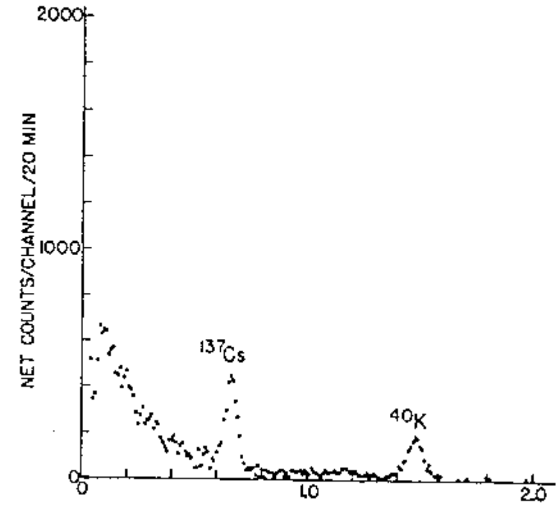
One of the patients studied in the whole-body counter was a child who has a nonfunctioning thyroid believed to have been caused by radioiodine therapy of the mother — a patient treated for cancer of the thyroid, who was given therapy before she was known to be pregnant. The child was shown to retain less than 1% of a tracer dose of ^{131}I three days after it was given. One of the main advantages of whole-body counting is that diagnostic tests can be done with very small amounts of radioactivity that are safe for children.

A visiting scientist from Japan, supported by the Picker Foundation, developed and built a color rescanner. Collaborators in the project included staff members of the Division, the Institute's Technical Services Department, and Oak Ridge National Laboratory.

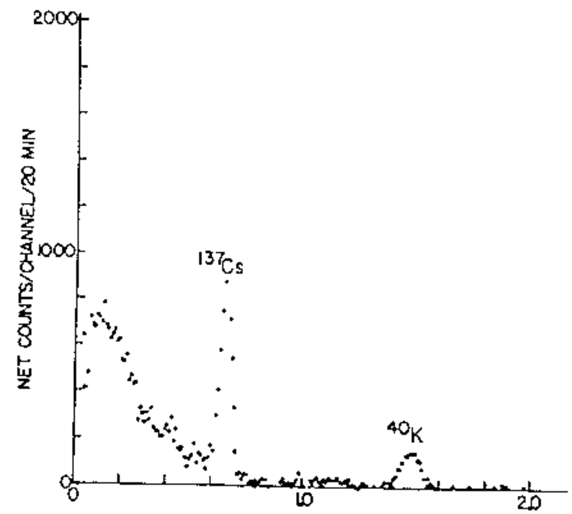
The rescanner produces a new record in color from an original scan made in black and white. The original scan, which shows the distribution of a radioisotope in a living patient, may be difficult to interpret because of the observer's difficulty in detecting small differences in density on the film. This may be particularly difficult in areas where the film is heavily exposed, but may have differences of exposure in areas that appear all black. The rescanner assesses the blackness of film through a densitometer and translates it into different colors that are easily apparent to the observer. As compared with a direct color scanner, which allows only one opportunity to control technical conditions, the rescanner allows repeated translation of the scan, with varying types of emphasis, into a satisfactory colored portrayal.

NASA Retrospective Study on Radiation Effects

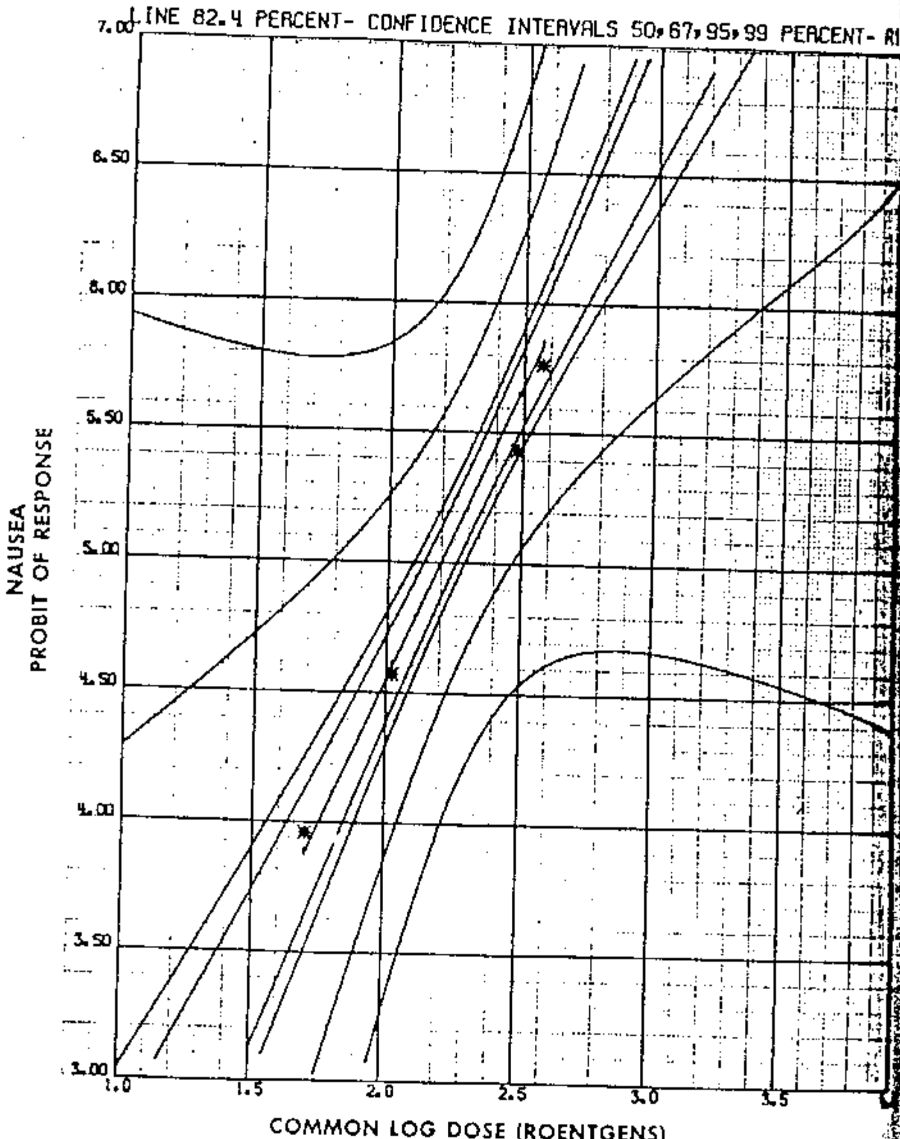
The Division continued to amass a large amount of information about radiation effects in the human being. This information is obtained from various clinical centers that have used total-body



Radioactivity spectrum obtained with the low-level whole-body counter from a normal man who drinks less than one pint of milk a day.



Radioactivity spectrum of a normal man who drinks more than one pint of milk a day showing higher amounts of ^{137}Cs (a fallout product) than in persons who consume low amounts of dairy foods.



Photography of machine-fitted regression lines charted directly by a computer from probit analyses to estimate the total-body irradiation dose required to produce a particular response in 50 per cent of patients. This is part of the study of radiat..n sensitivity in man being done for the National Aeronautics and Space Administration.

irradiation therapy in the human being, and from reports of radiation accidents. The record of each patient is very carefully coded by a method which takes into account factors of radiation dose, body size, and all types of clinical response and therapy. The most concentrated information is obtained for a period of six weeks after exposure. All this is handled by an elaborate data retrieval system which makes it possible to analyze the information in several different fashions. The fact that the system is open-ended allows continued addition of new cases. At least 1,000 patients have been given therapeutic total-body irradiation in the United States, and the objective is to obtain eventually information on all these patients.

The thoroughness of the study will make it possible to interpret the results in a way that has not been done before. For example, many clinical studies are handicapped by the fact that the underlying disease of the patient greatly influences the response to total-body irradiation. When comparisons are made with different groups of patients, adequate evaluation of these factors can be made, since some of the patients have very different diseases. Patients with renal failure being irradiated in preparation for a kidney graft do not have the underlying bone-marrow depression of the type that is seen in many patients with leukemia and lymphoma who are given total-body irradiation. Furthermore, the accident cases occurred in the main in people who were previously normal, and for this reason they are extremely informative, in spite of the fact that the dosimetry is often inadequate.

By combining all this information it is expected that more complete information about the effects of total-body irradiation in the human being can be obtained than has ever before been available.

TRAINEES IN CLINICAL INVESTIGATION

Peter Pfannenstiel — Germany
Elizabeth Ann Rush — Bonita Springs, Fla.
Masayuki Takasugi — Japan
Jaime J. Ahumada — Colombia, South America

JAMES PICKER FOUNDATION FELLOW

Guio Uchiyama — Japan

ABBOTT STUDENT FELLOWS IN NUCLEAR MEDICINE

Carl Drake, Jr. — Meharry Medical College, Nashville, Tenn.
Vernon Kraus — University of Cincinnati, Cincinnati, Ohio
Frederic Chin — St. Louis University, St. Louis, Mo.
Robert Douglas — University of Missouri, Columbia
Alan Ashare — Albany Medical College, Albany, N. Y.
Wallace Rogers — University of Minnesota Medical School, Minneapolis
Thomas Logan — Meharry Medical College, Nashville, Tenn.
Ira Jaffrey — State University of New York, Brooklyn

RESIDENT PHYSICIANS

Louis P. Mattoso — Massachusetts General Hospital, Boston
Dale Wenlund — Massachusetts General Hospital, Boston
Jack Wittenberg — Massachusetts General Hospital, Boston
Thomas Shea — Massachusetts General Hospital, Boston
George Zinninger — Massachusetts General Hospital, Boston
Gerald Kolodny — Massachusetts General Hospital, Boston
Gerald R. Summers — Baroness Erlanger Hospital, Chattanooga, Tenn.

INTERNATIONAL ATOMIC ENERGY AGENCY FELLOWS

Young Ja Lee — Korea
J. P. Goyal — India
Pedro N. Mendoza — Philippines

VISITING SCIENTIFIC GUESTS

Heinz Wahner — Colombia, South America
James Lim — University of North Carolina, Chapel Hill
Saido Rengell — Mexico

MEDICAL DIVISION CONFERENCES — 1964

July 2: Some uses of statistics — RAYMOND E. ROTH, professor and chairman, department of mathematics, St. Bonaventure University, Allegany, N. Y.

July 9: Plasmapheresis as a technique for transfusion of platelets, granulocytes, and stem cells — EMIL J. FREIREICH, medicine branch, National Cancer Institute, Bethesda, Md.

July 16: Cytogenetic studies in myeloproliferative disease—KONG-OO GOH, department of medicine, University of Rochester and Strong Memorial Hospital, Rochester, N. Y.

July 23: The rate of recovery of radiation injury in mice — JOHN STORER, assistant director for research, The Jackson Laboratory, Bar Harbor, Me.

July 23: Use of the analog computer in design of biologic experiments — ARTHUR L. KRETCHMAR, Division staff.

July 30: Dose in humans from internal emitters — RAYMOND L. HAYES, Division staff.

August 6: A review of gamma ray cameras for clinical use — A. C. MORRIS, JR., Division staff.

August 13: Studies on the effect of the level and nature of dietary fat on accumulative fat in bone marrow after total-body irradiation — JAMES N. BOLLINGER, Division staff.

August 20: Lipid metabolism in active hematopoietic cells and lipocytes — FRED SNYDER and REBA WRIGHT, Division staff.

August 27: Use of ^{131}iodine in serial tracers studies concerning the effect of TSH on the function of human normal and malignant thyroid tissue — PETER PFANNENSTIEL, University of Freiburg, Germany.

September 3: Problems in using the ORINS linear scanner for quantitative measurements — RALPH M. KNISELEY, Division staff.

September 10: Lanthanide colloidal preparations for bone marrow scanning — GRANVIL C. KYKER, Division staff.

September 17: Kinetic studies of rabbit muscle lactate dehydrogenase — VIRGINIA HOLTEN, biochemist, University of North Dakota School of Medicine.

September 23: Computer methodology in radioisotopic procedures — JOHN HIDALGO, biophysics laboratory, Tulane University.

September 24: Iodide and thyroxine turnover studies — T. H. ODDIE, Medical Center, University of Arkansas.

October 1: Possible uses of pi-mesons in biology and medicine — CHAIM RICHMAN, Graduate Research Center of the Southwest, Dallas, Tex.

October 8: A role for nutrition in cancer chemotherapy research—H. G. PETERING, biochemical research, Upjohn Company, Kalamazoo, Mich.

October 15: A method for comparing collimator systems applied to external counting of ^{51}Cr in the spleen — BILL M. NELSON, Division staff.

October 22: Some theoretical problems in biology — P.-E. E. BERGNER, Karolinska Institutet, Stockholm, Sweden.

October 29: Some pathologic aspects of the Rhode Island accident — C. C. LUSHBAUGH, Division staff.

November 5: Analytical applications of mass spectrometry — THOMAS NICHOLLS, Picker Nuclear.

November 9: The effect of thymectomy in the embryonic opposum upon hematologic and immune mechanisms — MATTHEW BLOCK, chief of hematology, University of Colorado Medical School.

November 12: Histopathological effects in animals exposed to heavy high energy charge particles — STUART W. LIPPINCOTT, research professor of pathology, Bowman Gray School of Medicine, Winston-Salem, N. C.

November 19: ^{131}iodine fibrinogen in the localization of tumors: a preliminary report — ANN RUSH, trainee in clinical investigation, Medical Division.

December 3: Application of neutron activation and radioautography to problems in experimental obesity — ALBERT F. DEBONS, assistant professor, department of surgery and physiology, Downstate Medical Center, Brooklyn, N. Y.

December 10: Summary report of Houston bone marrow recovery conference — ARTHUR L. KRETCHMAR and N. GENGOZIAN, Division staff.

December 17: Some factors governing the longevity of mammalian species — GEORGE A. SACHER, division of biological and medical research, Argonne National Laboratory.

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December 18: Prediction of lethality or other quantal end points for time-dependent patterns of radiation exposure — GEORGE A. SACHER, division of biological and medical research, Argonne National Laboratory.

MEDICAL DIVISION CONFERENCES — 1965

January 7: A molecular error-correcting mechanism — R. B. SETLOW, biology division, Oak Ridge National Laboratory.

January 14: Tissue typing — KONG-OO GOH, Division staff.

January 21: Clinical use of whole-body counter — RICHARD PETERSON, department of medicine, University of Iowa Medical School.

January 28: An introduction to nuclear counting statistics — ROGER J. CLOUTIER, Institute staff.

February 4: Localization of amino acids: some plans — RAYMOND L. HAYES, Division staff.

February 11: Presence of glyceryl ethers in tumors and bone marrow — FRED SNYDER, Division staff.

February 18: Nitrogen metabolism in irradiation chimeras — ARTHUR L. KRETCHMAR, Division staff.

February 23: Automatic analysis of the vectorcardiogram — F. STALLMANN, University of Tennessee.

February 25: Radioisotopic scanning of bone marrow in animals—GRANVIL C. KYKER, Division staff.

March 4: Estimation of effective doses of gastrointestinal responses to total-body irradiation in man — C. C. LUSHBAUGH, Division staff.

March 11: Mechanism of absorption and triglyceride biosynthesis in the intestinal mucosa — JOHN M. JOHNSTON, department of biochemistry, Southwestern Medical School, University of Texas.

March 18: Immunologic studies of the mechanism of action of erythropoietin — JOHN C. SCHOOLEY, Lawrence Radiation Laboratory.

March 25: Pre-leukemic state — MATTHEW BLOCK, University of Colorado Medical Center, Denver.

April 1: Report of the golden anniversary session of the American College of Physicians — RYOSAKU TANIDA, Division staff.

April 8: Qualitative and quantitative analysis of nucleic acid derivatives by chromatography and electrophoresis on thin-layers—KURT RANDERATH, John Collins Warren Laboratories of the Huntington Memorial Hospital, Harvard University.

April 15: Radioisotope techniques in the study of pulmonary function in health and disease — HENRY WAGNER, JR., associate professor, Johns Hopkins University Medical School.

April 22: Erythropoietin: laboratory and clinical studies—ROBERT D. LANGE, professor of research, University of Tennessee Memorial Research Center, Knoxville.

April 29: Preliminary design of a low-level, total-body therapeutic irradiator for man — ROGER J. CLOUTIER and PATRICIA DALTON, Institute staff.

May 6: Brain scanning — JOSEPH L. IZENSTARK, Emory University School of Medicine, Atlanta, Ga.

May 12: Studies of human hemoglobins — H. R. MARTI, Medizinische University Polyclinic, Basle, Switzerland.

May 13: Diseases in a laboratory colony of the primate, *Tamarinus nigricollis* — G. E. COSGROVE, pathologist, biology division, Oak Ridge National Laboratory, and BILL NELSON, Division staff.

May 20: Clinical use of the autofluoroscope — MERRILL A. BENDER, department of nuclear medicine, Roswell Park Memorial Institute, Buffalo, N. Y.

May 27: Reexamination of the rare earth-induced fatty liver — VIRGINIA HOLTEN, Division staff.

June 3: Bone scanning with gallium-68 — RAYMOND L. HAYES, Division staff.

June 10: On representation and prediction in biology — P. -E. E. BERGNER.

June 17: On epigenesis — WALTER M. ELSASSER, department of geophysics, Princeton University.

June 24: Bone marrow scanning in animals — GRANVIL C. KYKER, Division staff.

Special Training Division

The Division continued its broad base of regular course offerings, established to meet the increasing demand for training in the use of radioisotopes in the fields of medicine, industry and research, and to contribute to improvement of the professional competence of science teachers.

New programs were developed and this expansion included two major training presentations — participation in the International "Atoms at Work" exhibit sponsored by the U. S. Atomic Energy Commission, and the initial presentation of a nine-month academic year institute for high school teachers.

Twenty-two training courses were presented at the Division facilities, with a total of 445 participants. Since the establishment of the Division in 1948, 6,127 participants have attended 212 courses. Of these, 578 have been from 63 foreign countries.*

Radioisotope Course

The basic course in the application of radioisotopes in the areas of research, industry and engineering continued to be a successful program. Five courses, each lasting four weeks, were presented during the year. These were attended by 184 participants from 45 states, the District of Columbia, Puerto Rico and 16 foreign countries. Approximately 12 per cent of the 184 participants were not United States citizens.

This basic course is presented to give scientists and research workers intensive specialized training in the handling of radioisotopes and their utilization in research. Lectures and laboratory instruction are given in basic nuclear theory, instrumentation, radiation detection, radiological safety, and the interaction of radiation

**Argentina, Australia, Austria, Belgian Congo, Belgium, Brazil, Burma, Canada, Ceylon, Chile, China (Nationalist), Colombia, Costa Rica, Cuba, Denmark, Dominican Republic, Ecuador, Egypt, El Salvador, Finland, France, Germany, Great Britain, Greece, Guatemala, Iceland, India, Indonesia, Iraq, Iran, Ireland, Israel, Italy, Japan, Jordan, Korea, Lebanon, Luxembourg, Malaya, Mexico, Morocco, Netherlands, New Zealand, Nigeria, Norway, Pakistan, Panama, Peru, Philippines, Portgual, Senegal, Spain, Sweden, Switzerland, Syria, Thailand, Tunisia, Turkey, Union of South Africa, Uruguay, Venezuela, Viet Nam and Yugoslavia.*

Institute Board of Directors

Paul M. Gross, *President*
William Howell Pegram Professor of Chemistry,
Duke University
Eric Rodgers, *Vice President*
Dean of the Graduate School, University of Alabama
William W. Akers
Chairman, Department of Chemical Engineering,
Rice University
Jesse W. Beams
Francis H. Smith Professor of Physics,
University of Virginia
R. W. Brown
Vice President, Tuskegee Institute
H. W. Davis, *Chairman of the Council*
Dean of the College of Arts and Sciences,
University of South Carolina
M. E. DeBakey
Chairman, Department of Surgery,
College of Medicine, Baylor University
J. R. Dunning
Dean of the School of Engineering and Applied Science,
Columbia University
George T. Harrell
Dean, Milton S. Hershey Medical Center,
Pennsylvania State University
Warren C. Johnson
Vice President in Charge of Special Scientific Programs,
University of Chicago
Robert T. Lagemann
Chairman, Department of Physics and Astronomy,
Vanderbilt University
Clarence E. Larson
President, Nuclear Division, Union Carbide Corporation
Charles T. Lester
Dean of the Graduate School of Arts and Sciences,
Emory University
Simon H. Wender
Research Professor of Chemistry, University of Oklahoma
John L. Wood
Chairman, Department of Biochemistry,
University of Tennessee at Memphis

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Sponsoring Institutions

Sponsoring institutions and their representatives on the Council are:

Auburn University .... *W. V. Parker*
Catholic University of America .... *Francis L. Talbott*
Clemson University .... *H. L. Hunter*
Duke University .... *Lewis Anderson*
Emory University .... *Robert B. Platt*
Fisk University .... *J. R. Lawson*
Florida State University .... *Russell J. Keirs*
Georgia Institute of Technology .... *M. J. Goglia*
Louisiana State University .... *R. C. Keen*
Medical College of Virginia .... *F. T. O'Foghludha*
Meharry Medical College .... *Isaac H. Miller*
Mississippi State University .... *E. Irl Howell*
North Carolina State University .... *A. C. Menius, Jr.*
North Texas State University .... *R. B. Escue*
Rice University .... *Gerald C. Phillips*
Southern Methodist University .... *W. B. Stallcup*
Texas A & M University .... *John A. McIntyre*
Texas Christian University .... *Joseph Morgan*
Texas Woman's University .... *John A. Guinn*
Tulane University .... *Joseph C. Morris*
Tuskegee Institute .... *James H. M. Henderson*
University of Alabama .... *Frederick W. Conner*
University of Arkansas .... *L. F. Bailey*
University of Florida .... *George K. Davis*
University of Georgia .... *G. B. Huff*
University of Kentucky .... *W. C. DeMarcus*
University of Louisville .... *R. C. Ernst*
University of Maryland .... *M. J. Pelczar*
University of Miami .... *Maxwell Dauer*
University of Mississippi .... *F. A. Anderson*
University of North Carolina .... *H. C. Thomas*
University of Oklahoma .... *Lawrence M. Rohrbaugh*
University of Puerto Rico .... *Juan D. Curet*

6/30/66

Annual Report

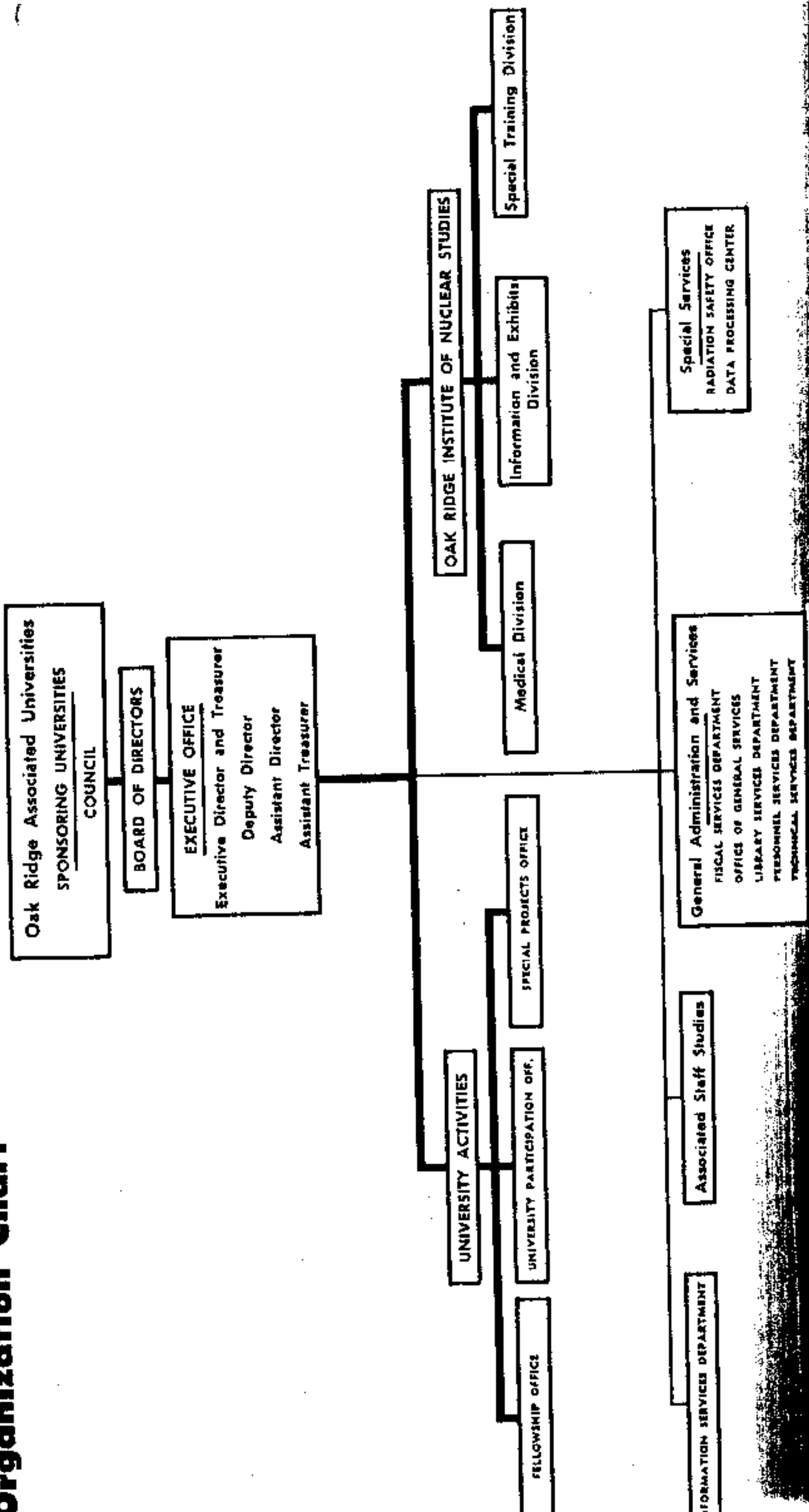
First • Oak Ridge Associated Universities

Twentieth • Oak Ridge Institute of Nuclear Studies

OPERATING UNDER CONTRACT WITH
UNITED STATES ATOMIC ENERGY COMMISSION

JUNE 30, 1966

Table of Contents



Organization Chart

Foreword

A CHARTER of incorporation for Oak Ridge Associated Universities (then called Oak Ridge Institute of Nuclear Studies) was issued by the State of Tennessee on October 15, 1946. It was registered with the County Court Clerk of Anderson County in Clinton, Tenn., on October 16, 1946. The first official meeting of the membership of the new corporation was held the following day. The five incorporators—Frank P. Graham, Paul M. Gross, Paul W. McDaniel, William G. Pollard and Francis G. Slack—met and adopted bylaws for the corporation, elected in accordance with these bylaws 14 universities to membership, and then submitted their resignations as members of the corporation. Since then, the only members of Oak Ridge Associated Universities have been universities in the Southern region of the United States. With subsequent additions, members of the corporation now number 40.

This report has been prepared for presentation by the Board of Directors of O.R.A.U. to the Council representatives and presidents of member institutions at a twentieth anniversary banquet to be held on October 17, 1966, just 20 years from the first organizational meeting of the corporation. It seems appropriate, therefore, to review here the background and significance of our organizational structure.

One of the greatest strengths of the Association is its widely representative character, including in its corporate membership nearly all the major institutions of higher learning offering graduate work in science in the South and Southwest. Each of the 40 member institutions is represented on a body called the Council. The Council elects the Board of Directors and adopts corporate bylaws. Unlike many other corporations, however, the Council does much more. The entire Council is divided into committees which meet during the year, somewhat in the capacity of a "board of visitors," to examine in detail various aspects of the Association's operations and programs. These committees report to the Council and frequently make recommendations to the Board of Directors which are of great value in keeping O.R.A.U. programs as responsive as possible to the wishes of its member institutions.

The chart on Pages 12-13 shows the member institutions and the names of those persons who have represented them on the Council throughout the 20-year period. The interest and enthusiasm of the Council representatives in the welfare of the Association, and their energy in making its programs effective in their institutions, have been a great source of strength. Outside observers, as well as members of the Council, frequently have commented on the good will which has been a notable mark of the Council throughout its history.

In addition to the Council members, under a program initiated this year, member institutions maintaining two or more campuses may appoint up to two additional representatives. These Campus Representatives handle O.R.A.U. affairs on the branch campus in the same way as the Council member does on the main campus. Campus Representatives serve on Council committees and attend the annual meeting of the Council, but do not vote. The present campus representatives include:

Louisiana State University, Medical Center, New Orleans—*E. A. Daigneault*
Louisiana State University in New Orleans—*Mary L. Good*
University of Alabama, Medical Center, Birmingham—*Charles Kochakian*
University of Arkansas, Medical Center, Little Rock—*H. N. Marvin*
University of Mississippi, Medical Center, Jackson—*R. D. Sloan*
University of Oklahoma, Medical Center, Oklahoma City—*G. D. Adams*
University of Tennessee, Medical Units, Memphis—*R. H. Alden*
University of Texas, Texas Western College, El Paso—*L. L. Abernethy*
University of Texas, Southwestern Medical School, Dallas—*Frank Harrison*

Another strength of the Association is the quality and competence of those who serve on its Board of Directors. Members of the Board serve without compensation and carry a heavy management responsibility. The Association's long record of sound and effective management and financial integrity attests to the effectiveness with which the Board has functioned. The accompanying list of officers and directors of O.R.A.U. since its incorporation (Pages 10-11) shows how fortunate the Association has been in attracting men of distinction during these 20 years.

Oak Ridge Associated Universities was the first university corporation established in the United States for the purpose of operating scientific and educational programs under government contract. Within six months, a second such corporation, Associated Universities Incorporated, was formed in the Northeast, and for several years O.R.A.U. and AUI were the only two such corporations in the country. A considerable number of such corporations, both regional and national, now have been formed. The multi-

university operating and management corporation has become an established element in the American academic scene and is extensively used by government agencies to carry out important national research and development programs.

A comment which has been made with some frequency about the O.R.A.U. structure is that the number of member universities may be too large to ensure long-term stability for undertaking large scale operations under government contract. It is argued that a small number of leading universities would be preferable because the Atomic Energy Commission or other agencies would have only this small group of strong institutions with which to deal.

The fallacy in this argument is that in no event does the contracting agency deal with the individual universities in a multi-university corporation, any more than it deals with individual stockholders of any of its industrial contractors. Whether the corporate membership is small and select, or broadly representative and diverse, it is the Board of Directors which has management responsibility, enters into contracts, and with which the government agency discusses major problems.

The long-term stability of such a corporation for undertaking large scale operations under contract thus rests not on the size or character of the institutional membership, but on whether its method of choosing a Board of Directors gives assurance of management competence.

The O.R.A.U. method of providing such assurance involves the use of a nominating committee, three members of which—including the chairman—are elected each year by the entire Council from its own membership. Two others, elected by the Board of Directors, are from member institutions. The nominating committee presents enough nominations to give the Council choices in filling vacancies on the Board, and the final selections are made by majority vote of the entire Council. Since the only nominees are those presented by this committee, it is not possible for the weaker institutions to gain control of any Board position over the stronger institutions. The quality of the Board of Directors produced by this method is attested by the names of those who have served on the Board over a 20-year period.

A small, select institutional membership, on the other hand, would give the corporation the character of an aristocracy with which the majority of institutions in the region would not identify. The broadly representative character of the membership of O.R.A.U. makes it truly an expression of the aims and aspirations of the whole of graduate education in science of the region. No element feels excluded and the whole region shares the feeling of pride and satisfaction in the achievements of the Association. This is a great strength which has proved itself over 20 years and should certainly be retained in the future.

A unique feature of O.R.A.U. has been its relationship to Oak Ridge National Laboratory. The Oak Ridge pattern has been different from that of other national laboratories in the United States in that ORNL has always been operated by an industrial contractor; first by Monsanto Chemical Company, and since 1948 by Union Carbide Corporation. O.R.A.U. has a separate prime operating contract with the Atomic Energy Commission which is essentially the same as the one between the Commission and Union Carbide for the operation of ORNL. Although there has never been any contract or legally binding agreement between O.R.A.U. and Union Carbide, extensive programs for research participants, Oak Ridge graduate fellows, traveling lectures, summer student trainees, and others have been carried out effectively between them throughout the 20-year period. This wedding of an industrial contractor with a university corporation in extensive programmatic responsibilities has proved to be a strong and effective arrangement, although its workability often has been mystifying to those in other regions. A further element in strengthening this relationship has been the election by the Council since 1949 of a representative of Carbide to the O.R.A.U. Board of Directors.

This relationship was extended this year to other areas through a sizable manpower training program at the Oak Ridge Y-12 Plant, which also is operated by Union Carbide. This unusual and important demonstration program in skill training was developed and implemented by O.R.A.U. with the cooperation of Union Carbide and the University of Tennessee. The actual training is being provided by Union Carbide instructors in the Y-12 facilities, and by the University of Tennessee which is providing significant services to vocational and technical teachers participating in the program.

The use of industrial facilities to expand the manpower training potential of the nation may well become widespread as a result of this demonstration. The program, described in greater detail in this report, is a dramatic example and extension into another area of the fruitful relationship between Union Carbide and O.R.A.U. in the joint operation of major programs.

Another new program which demonstrates the broad potential strength of a multi-university corporation with experience in the management of programs under government contract is the summer student internship program described in detail in this report. Here, the background of ex-

perience gained in the administration of the Summer Student Trainee program at Atomic Energy Commission laboratories in Oak Ridge and Savannah River has been extended to the administration of a similar program in resource development. Selected university students are assigned projects to be carried out in the field, working closely with resource development agencies or community action committees under the guidance of a professor in their university. The government agencies supporting the program transferred the funds for it to the Atomic Energy Commission and O.R.A.U. administers the program under its Atomic Energy Commission contract.

The many and varied programs covered in this report represent another year of growth and achievement for Oak Ridge Associated Universities. The formation of this Association 20 years ago has paid many dividends in important scientific and educational achievements, not only for its sponsoring institutions, but for the nation as a whole. The wisdom of the university representatives who decided late in 1945 to create such an entity is amply demonstrated in this report.

William G. Pollard

Officers of Oak Ridge Associated Universities

Since Its Incorporation

Frank P. Graham
President
1946-1949

Paul M. Gross
President
1949-present

VICE PRESIDENTS

Frederick Seitz, 1946-1949
J. W. Beams, 1949-1954
Clifford K. Beck, 1954-1956
Marten tenHoor, 1956-1957
Warren C. Johnson, 1957-1959
Louis A. Pardue, 1959-1963
Howard M. Phillips, 1963-1965
Eric Rodgers, 1965-present

William G. Pollard
Secretary-Treasurer (Executive Director)
1946-present

CHAIRMEN OF THE COUNCIL

Frank P. Graham, 1946-1949
J. Harris Purks, 1949-1950
Louis A. Pardue, 1950-1952
George H. Boyd, 1952-1955
Marten tenHoor, 1955-1958
Robert T. Lagemann, 1958-1961
Simon H. Wender, 1961-1964
H. Willard Davis, 1964-present

BOARD OF DIRECTORS

W. W. Akers, 1963-present
William R. Arrowsmith, 1961-1964
Sanford S. Atwood, 1965-present
Ronald Bamford, 1957-1964
J. W. Beams, 1946-1954; 1960-present
Clifford K. Beck, 1953-1956
Tom W. Bonner, 1959-1962
George H. Boyd, 1952-1955
B. W. Brown, 1962-present
George L. Cross, 1954-1957
Harry A. Curtis, 1957-1960
Joseph M. Dallavalle, 1955-1958
H. Willard Davis, 1964-present
Michael E. DeBakey, 1964-present
Karl Dittmer, 1965-present
Charles E. Dunlap, 1955-1962
John R. Dunning, 1950-1959; 1962-present
Henry J. Gomberg, 1959-1962
Ernest W. Goodpasture, 1946-1952
Frank P. Graham, 1946-1949
Paul M. Gross, 1946-present
George T. Harrell, 1954-1960; 1963-1965
Leland J. Haworth, 1959-1961
William V. Houston, 1951-1958
Warren C. Johnson, 1953-1959; 1961-present
Robert T. Lagemann, 1958-present
Clarence E. Larson, 1953-1955; 1962-present
Charles T. Lester, 1962-1965
David E. Lilienthal, October and November 1946
Samuel C. Lind, 1949-1953
Edward Mack, 1950-1952; 1954-1956
Hayden C. Nicholson, 1952-1955
T. S. Painter, 1947-1953
Louis A. Pardue, 1950-1955; 1956-1963
George B. Pegram, 1946-1949
Merlin D. Peterson, 1953-1959
Carl C. Pfeiffer, 1955-1958
Howard M. Phillips, 1958-1964; 1965-present
William G. Pollard, 1946-1948
Russell S. Poor, 1948; 1960-1962
J. Harris Purks, 1949-1950; 1954-1957
Eric Rodgers, 1963-present
Frederick Seitz, 1946-1949
Arthur H. Snell, 1959-1962
Herman E. Spivey, 1965-present
Harold W. Stoke, 1949-1951
Marten tenHoor, 1955-1962
James E. Webb, 1956-1960
H. Stephen Weeks, 1960-1963
Alvin M. Weinberg, 1955-1959
Simon H. Wender, 1961-present
Eugene P. Wigner, 1947-1948
John L. Wood, 1958-1965

Member Institutions of Oak Ridge Associated Universities and Councilors
1946-1966

	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66
AUBURN UNIVERSITY	R. S. Poor			Fred Allison				William Vann Parker													
CATHOLIC UNIVERSITY OF AMERICA	Karl F. Herzfeld								George D. Rock										F. L. Talbott		
CLEMSON UNIVERSITY							Howard L. Hunter														
DUKE UNIVERSITY	Walter M. Nielsen														Karl M. Wilbur						1
EMORY UNIVERSITY	J. Harris Purks				2	J. G. Stipe		H. M. Phillips			C. T. Lester						R. B. Platt				
FISK UNIVERSITY													James R. Lawson								
FLORIDA STATE UNIVERSITY						Milton W. Carothers							W. A. Baum				R. J. Keirs				
GEORGIA INSTITUTE OF TECHNOLOGY	3		R. L. Sweigert													Mario J. Goglia					4
LOUISIANA STATE UNIVERSITY	Richard C. Keen																				
MEDICAL COLLEGE OF VIRGINIA																		5	F. T. O'Foghludha		
MEHARRY MEDICAL COLLEGE										Paul F. Hahn					Isaac H. Miller						
MISSISSIPPI STATE UNIVERSITY				Mahlon P. Etheredge															E. I. Howell		
NORTH CAROLINA STATE UNIVERSITY				6	Clifford K. Beck			7	F. Phillips Pike						R. Murray		A. C. Menius				
NORTH TEXAS STATE UNIVERSITY										J. C. Matthews			Richard B. Escue								
RICE UNIVERSITY				Tom W. Bonner										William W. Akers				Gerald C. Phillips			
SOUTHERN METHODIST UNIVERSITY								Wayne Rudmose										J. L. McCarthy			
TEXAS A & M UNIVERSITY							D. H. Morgan			Donald F. Weekes										J. McIntyre	
TEXAS CHRISTIAN UNIVERSITY																	Joseph Morgan				
TEXAS WOMAN'S UNIVERSITY															John A. Guinn					K. A. Fry	
TULANE UNIVERSITY	J. C. Morris		Robert T. Nieset													J. C. Morris					

1. Lewis Anderson
2. Robert T. Lagemann
3. Robert I. Sarbacher
4. E. A. Trabant
5. E. Richard King
6. C. G. Brennecke
7. C. G. Brennecke

	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66
TUSKEGEE INSTITUTE								R. W. Brown									James H. M. Henderson				
UNIVERSITY OF ALABAMA	8	Marten tenHoor											Eric Rodgers					F. W. Conner			9
UNIVERSITY OF ARKANSAS			W. W. Grigorieff					R. R. Edwards			Lowell F. Bailey										
UNIVERSITY OF FLORIDA			Roland B. Eutsler								R. S. Poor				George K. Davis					10	
UNIVERSITY OF GEORGIA			George H. Boyd											Gerald B. Huff							
UNIVERSITY OF KENTUCKY	11		12		Lyle R. Dawson						13			Wendell C. DeMarcus							
UNIVERSITY OF LOUISVILLE			Robert C. Ernst																		
UNIVERSITY OF MARYLAND						Ronald Bamford					14			Michael J. Pelczar							
UNIVERSITY OF MIAMI											Walter O. Walker						Maxwell Dauer				
UNIVERSITY OF MISSISSIPPI			15	P. K. McCarter				16		Frank A. Anderson											
UNIVERSITY OF NORTH CAROLINA	Frank P. Graham			C. D. VanCleave							Arthur Roe			Henry C. Thomas							
UNIVERSITY OF OKLAHOMA				L. H. Snyder			Simon H. Wender												L. M. Rohrbaugh		
UNIVERSITY OF PUERTO RICO						Facundo Bueso									Juan D. Curet						
UNIVERSITY OF SOUTH CAROLINA					H. Willard Davis																
UNIVERSITY OF TENNESSEE	F. C. Smith		E. A. Waters								Hilton A. Smith										
UNIVERSITY OF TEXAS	T. S. Painter				C. P. Boner			Malcolm Y. Colby					R. N. Little								
UNIVERSITY OF VIRGINIA	17	L. B. Snoddy			John H. Yoe													E. R. VanArtsdalen			
VANDERBILT UNIVERSITY	18	Philip Davidson				19		Robert T. Lagemann								20	21	Oscar Touster			
VIRGINIA POLYTECHNIC INSTITUTE				22	L. A. Pardue			Frank C. Vilbrandt					R. C. Krug							23	
WEST VIRGINIA UNIVERSITY											R. B. Dustman				24	John F. Golay					25

8. James R. Cudworth
9. Earl A. Long
10. Billy G. Dunavant
11. W. D. Funkhouser
12. Louis A. Pardue
13. Lewis W. Cochran
14. Nathan L. Drake
15. J. D. Williams
16. Fred W. Kellogg
17. L. G. Hoxton
18. Harvie Branscomb
19. Merlin D. Peterson
20. Leonard B. Beach
21. Graham DuShane
22. C. Clement French
23. Fred W. Bull
24. Walter A. Koehler
25. Robert S. Dunbar

20 Years of Progress

THERE IS an old story about the motion picture whose opening credits stated, in part: "Screen Play by John Doe and Richard Roe, Based Upon a Chance Remark by Samuel Goldwyn."

It is at least mildly astonishing, in looking back after 20 years of outstanding accomplishment, to realize that the origin of Oak Ridge Associated Universities was almost as fortuitous—the result of an animated conversation at a social gathering in Knoxville, Tennessee.

The occasion was a party given by Dr. and Mrs. Robert M. Boarts of the University of Tennessee for Katherine Way, a former member of the University of Tennessee physics staff, at that time working at the Metallurgical Laboratory of the University of Chicago. The party was an informal get-together to provide Dr. Way with an opportunity to visit with some of her old friends. The time was September 1945, little more than a month after the world had become aware of the existence of Oak Ridge—the "secret city" of World War II that was the site of the tremendous installations that played such a vital part in ushering in the fantastic new "Atomic Age."

It was only natural that, in a group of science-faculty members, nuclear energy and the Atomic City should play a prominent part in the conversation. One of the members of the group was William G. Pollard, a University of Tennessee physics professor recently returned to his university post after spending the wartime years with the Columbia University team working on development of the gaseous diffusion process for the separation of uranium isotopes.

The spark was struck when Dr. Way made a suggestion to Dr. Pollard: Wouldn't it be wonderful if the great nuclear energy facilities at Oak Ridge could be made available to the scientific staffs of Southern universities as a tremendous educational tool that would not only benefit the universities, but greatly implement the peacetime nuclear research and development programs of the entire nation?

The suggestion led to an intense and lengthy discussion, with mixed reactions. An initial postulation that such a program might be undertaken by the University of Tennessee, supported by an institutional grant, or contributions from Southern universities interested in participating, was tempered by the possibility that a project of such scope would be too great for a single university to manage. The following day, Dr. Pollard discussed the problem with Kenneth L. Hertel, head of his department, and the two men then conferred with Fred C. Smith, dean of the University of Tennessee.

The first result of these discussions was the preparation of "A Proposal for the University of Tennessee Sponsorship of Basic Research," submitted for the consideration of Dean Smith and University of Tennessee President James D. Hoskins. It was accompanied by another document entitled "Basis for Collaboration Between Monsanto Chemical Company and the University of Tennessee in a Research Institute." Monsanto at that time operated the Clinton Laboratories in Oak Ridge under contract with the Manhattan District of the U. S. Army Corps of Engineers—the organization responsible for carrying out the wartime atomic energy project. Drs. Pollard, Hertel and Boarts were also constituted by President Hoskins as a committee to carry on with the project.

Coincidentally, M. D. Whittaker, director of Clinton Laboratories, and Warren Johnson, head of its Chemistry Division, had approached the University of Tennessee staff members to discuss the possibility of a program of graduate courses at the Laboratories taught by Laboratories staff members approved by the University. Approval of this program by the University of Tennessee resulted in several members of the University staff wearing two hats: involvement in the new Oak Ridge educational facility project and the graduate program at Clinton Laboratories. It is not surprising that the latter program eventually became an important part of the former—the first courses, held during the 1946 fall quarter, later developed into the Oak Ridge Resident Graduate program.

Meanwhile, the Pollard-Boarts-Hertel committee embarked on a series of intensive meetings and discussions in Washington, D. C., and in Tennessee, with congressmen; top-ranking officials in the Navy Department and the Army, including General Leslie R. Groves, wartime director of the Manhattan District; university executives; and David Lilienthal, chairman of the Tennessee Valley Authority.

Subsequent meetings involving representatives of the University of Tennessee and Clinton Laboratories resulted in an invitation to the Universities of Kentucky, Virginia, North Carolina, Tennessee, and Chattanooga; Emory and Vanderbilt Universities; and Alabama and Virginia Polytechnic Institutes, for a conference in Knoxville on December 5, 1945. This meeting led to another in Oak Ridge on December 27-29, attended by representatives of the three major Oak Ridge installations—Carbide and Carbon Chemicals Company, Tennessee Eastman Company, and Clinton

Laboratories—as well as academic representatives from an expanded group of universities.

From this last conference came the appointment of an Executive Committee, headed by Dr. Pollard, to study various phases of the proposed program and a formal name for the new organization: The Oak Ridge Institute of Nuclear Studies.

The committee immediately undertook planning and arranging two major programs: one, under which graduate students and university faculty members could come to Oak Ridge to participate in research programs; the other, a program by which young scientists employed in Oak Ridge could work toward their masters' and doctors' degrees without leaving their positions to return to school. Both programs were put into effect even before the formal chartering of the Institute and, as the Oak Ridge Research Par-

The first meeting of the ORINS Council was held on October 17, 1946. Clockwise around the table are: W. M. Nielsen, Duke University; J. Harris Purks, Jr., Emory University; Francis J. Slack and Harvie Branscomb, Vanderbilt University; Robert I. Sarbacher, Georgia Institute of Technology; J. C. Morris, Tulane University; Robert H. Marquis and John P. Ferris, Tennessee Valley Authority; Karl F. Herzfeld, Catholic University of America; William G. Pollard, then of the University of Tennessee; and Frank P. Graham (standing), first president of the corporation. Not shown in the photograph but present at the meeting were: Russell S. Poor, Alabama Polytechnic Institute; J. D. Cudworth, University of Alabama; and Fred C. Smith, University of Tennessee.

ticipation program and Oak Ridge Graduate program, are still important activities of Oak Ridge Associated Universities.

As to the organization of the new Institute, itself, the Executive Committee, after much study and discussion formulated a proposal for ORINS to incorporate as a nonprofit, educational corporation, whose membership would be composed of universities and colleges in the Southern region. Letters of invitation were sent out, in October, 1946, to universities recommended by the Conference of Deans of Southern Graduate Schools, requesting their attendance at a Council meeting on October 17. Actual incorporation was completed on October 16, with 14 universities represented as charter members. The incorporators met, adopted bylaws, and elected the representative institutions to corporate membership. The first Council meeting was then convened and elected the first Board of Directors. The Oak Ridge Institute of Nuclear Studies was launched.

The maiden voyage, however, was not a perfectly smooth one. A presidential order dissolved the Manhattan District and turned over all of its facilities to the new, civilian Atomic Energy Commission as of January 1, 1947. So, all the work that had gone into setting up a contract with the Manhattan District had to be carried out again with the new agency.

This was accomplished, an interim letter contract between ORINS and the AEC established the Institute as a prime contractor of the Commission, office space was provided, and the task of building up the organization got under way. Employees were hired, financial arrangements were worked out with the Commission, and plans were developed for carrying out the Institute's proposed programs of graduate fellowships, research participation, and a radioisotope techniques school.

Whereupon, Monsanto Chemical Company announced it was withdrawing as operating contractor of Clinton Laboratories, and new plans had to be made for ORINS operations. The fledgling Institute offered to assume operation of the Laboratories, and submitted a proposal to the AEC, but the Commission's decision was to place the University of Chicago in charge, and once more negotiations were undertaken to clarify the position of ORINS in the new setup.

Then, in the midst of the new negotiations, the AEC announced that the University of Chicago was withdrawing as operating contractor of Clinton Laboratories; that Carbide and Carbon Chemicals Company, which already operated the gaseous diffusion and electromagnetic separation plants, would assume operation of the Laboratories; and that a high-flux research

reactor planned for and designed at Clinton Laboratories would be built elsewhere.

Yet this situation, too, cleared up. Following Carbide's assumption of operation of Clinton Laboratories, the name was changed to Oak Ridge National Laboratory (ORNL), negotiations were undertaken for mutual programs involving ORNL and ORINS, and a working arrangement between the two institutions was developed that has been operating smoothly and effectively ever since.

By 1948, the new Institute was firmly entered upon the career of service, growth and expansion it has followed to this date. The field of nuclear education was new and unexplored. At almost every turn, new opportunities arose for the activation of programs peculiarly suited to the new organization. In 1948, ORINS assumed three major Atomic Energy Commission programs that resulted in the formation of a major divisional organization within the Institute.

The Atomic Energy Commission, besieged by requests to train scientific personnel at institutions throughout the country in the use of radioisotopes, arranged with ORINS to set up and operate a series of radioisotope techniques courses on a continuous basis. Concurrently, the AEC also suggested that the Institute undertake the establishment and operation of a research facility to study the uses of radioactive material in the diagnosis and treatment of cancer and other diseases. And the graduate fellowship and research participation programs, the cornerstones on which the Institute was founded, had developed into activities of national, as well as of regional, importance. Consequently, these three major programs were assigned to three separate divisions: Special Training, Medical and University Relations.

The formation of a fourth major division in 1949 was the result of the Atomic Energy Commission's decision to open up the residential area of Oak Ridge to the general public. Faced with the fact that there was nothing "atomic" for the public to see in the Atomic City, the Commission asked ORINS to set up a museum that would house artifacts of the nation's nuclear research programs and explain the new force in easy-to-understand terms. The proposal was studied, presented to the ORINS Board of Directors at its February 1949 meeting, adopted by the Board, and authorization was given for the formation of a Museum Division—now the Information and Exhibits Division—to undertake a suitable program. In the amazingly short time of five weeks, an abandoned cafeteria building was remodeled, a variety of exhibit materials was borrowed, designed and constructed; and

The first long-term contract between the Oak Ridge Institute of Nuclear Studies and the U. S. Atomic Energy Commission was signed on May 24, 1948. Shown at the signing are, from left, Herman M. Roth, Atomic Energy Commission; William G. Pollard, ORINS; and John C. Franklin, Manager, Oak Ridge Operations, Atomic Energy Commission.

when the Atomic City opened its doors to the public on March 19, 1949, so did the American Museum of Atomic Energy—now one of East Tennessee's outstanding tourist attractions.

The organizational setup of ORINS into four main divisions, with executive, administrative and service departments, is one that remained in effect for more than 15 years.

During that period, the Institute never failed to progress and expand in its major programs of providing education and information in all fields of nuclear energy to persons at every educational level, from the "man in the street" to the Ph.D., and not only on a regional basis, but on a national and international scale.

The University Relations Division, for example, took over the administration of Atomic Energy Commission fellowships in nuclear science and engineering, health physics and industrial hygiene, and, for a short period, the predoctoral fellowship programs for the Southeastern region of the United States. The Oak Ridge Research Participation program provided

research opportunities in Oak Ridge and other Atomic Energy Commission installations for science faculty members of universities and colleges throughout the nation. A "traveling teacher" program, designed to stimulate interest in science and science teaching careers on the part of high school students by sending specially trained science teachers to high schools throughout the nation, developed into a regular series of training courses for teachers and administrators in state school systems. An outgrowth of this program has been the operation of special seminars for science teachers in Europe, Asia, and South and Central America as part of the Atomic Energy Commission's overseas traveling exhibit, "Atoms in Action." The program includes training teachers in Oak Ridge in preparation for conducting the special courses in their home countries during the showing of the exhibit.

A student trainee program was initiated that regularly brings outstanding college science students at the rising-senior level to Oak Ridge and the Savannah River Laboratory, Aiken, S. C., during the summer months to engage in research projects, under the supervision of outstanding scientists.

The University Relations Division was also responsible for a series of special symposia and conferences in Oak Ridge and at member institutions, and for the establishment of the Oak Ridge Traveling Lecture program that sends Oak Ridge scientists to campuses in the Southern region to hold seminars and discussions on a wide variety of topics in the field of nuclear energy.

The Special Training Division, which started out by presenting basic courses in radioisotope techniques, expanded its curriculum to where it now presents a wide variety of courses each year to hundreds of scientists from all over the world as well as the United States. The roster includes isotope applications to industry, medicine, highway engineering, ecology, health physics, botany and other fields. To date, the Division has provided training to more than 6,000 scientists and engineers from all 50 states of the Union, its territories, and 60 foreign countries.

In addition to the courses presented in Oak Ridge, the Special Training Division also operates three mobile laboratories—large vans containing small but well-equipped facilities that visit colleges throughout the United States to provide intensive, two-week radioisotope techniques courses to faculty members and students who might otherwise be unable to participate in such work.

The Medical Division has been extremely active in the development of programs connected with the medical applications of radioactivity. It has tested scores of radioisotopes as diagnostic and therapeutic agents in a variety of diseases and bodily disorders; operates a 34-bed hospital and an extensive outpatient service; has designed and developed an extensive series of scanning, brachytherapy and teletherapy devices; conducts an intensive preclinical program; a study of immunology in a special type of primate; and provides regular instruction, through residencies, courses and conferences, in applications of radioisotopes to the detection and treatment of diseases.

Shortly after it began operation of the American Museum of Atomic Energy, the Information and Exhibits Division was also assigned the administration of the AEC's domestic traveling exhibits program. Each year, these exhibits, ranging from unmanned "package" displays to large, manned units designed for extended showings at museums, fairs and other large convocations, bring the message of the peaceful atom to many millions of persons throughout the country who have never seen the American Museum of Atomic Energy, and to whom Oak Ridge is merely the name of a city.

This proliferation of programs and activities naturally brought about a need for an increased staff and a concomitant need for expanded facilities. For ten years, such facilities were provided by the Atomic Energy Commission. On the occasion of the celebration of the tenth anniversary of the founding of ORINS, the Institute took a major step in its development:

An informal ceremony was held in connection with the groundbreaking for the Central Administration Building on February 19, 1959.

the purchase, with Institute funds, of some 38 acres of land in Oak Ridge on which it subsequently built the present Central Administration Building and Library Building, with ample space for other facilities now in the planning stage.

This development, which for the first time in its existence permitted the Institute to develop and carry out programs of research and training in buildings and with facilities not owned by the Atomic Energy Commission or other governmental agency, led to a corresponding widening of interest in conducting programs not necessarily or directly concerned with Commission activities.

When the Oak Ridge Institute was formed, its principal interest was in utilizing the nuclear facilities in the Atomic City to improve the science teaching and research programs in Southern institutions of higher learning--hence, the incorporation of the term "Nuclear Studies" into the title. At the time, it was not clear what role the organization might play in the postwar development of nuclear science. Later, as the scope of the programs and activities that ORINS undertook for the Atomic Energy Commission widened, it became increasingly clear that its corporate name was not strictly descriptive of its activities or functions.

For example, the Institute designed and constructed a special children's exhibit, "Atomsville, U.S.A.," as part of an AEC presentation at the New York World's Fair in 1964-65. The University Relations Division conducted a series of special conferences on science and the humanities under joint sponsorship of the U. S. Atomic Energy Commission and other organizations. The Medical Division undertook a retrospective survey of radiation damage to human beings for the National Aeronautics and Space Administration, and participated with Oak Ridge National Laboratory in a study for the National Institutes of Health of virus particles associated with leukemia. This, in turn, led to the establishment of a Data Processing Center in the Division to collect, store and process information on whole-body radiation, and the Center's facilities were later extended to provide services to other research activities of the Institute.

Finally, in 1965, ORINS undertook a survey of manpower training resources and needs in 15 Southern states under a six-month project for the U. S. Department of Labor.

It was obvious that, since ORINS' growth was exceeding the semantic limits of "nuclear studies," it was necessary to make some change in the corporation's title that would properly reflect its position in the field of education and research, and to revise its operational structure to conform and adapt to changing conditions.

Accordingly, at a meeting of the presidents of the ORINS sponsoring institutions in March 1965, recommendation was made and approved that the corporate name be changed to "Oak Ridge Associated Universities." This recommendation was passed on by the Council at its October meeting, and the change of name became official on January 1, 1966.

In preparation for the changeover, a major organizational change was also effected. The Oak Ridge Institute of Nuclear Studies did not pass out of existence, but was maintained as an operating unit of Oak Ridge Associated Universities, comprising the Special Training, Medical and Information and Exhibits Divisions, which continue to carry out their regular programs. The University Relations Division was dissolved; in its place, three offices

This aerial view shows the Central Administration Building and Library Building of Oak Ridge Associated Universities.

were established which operate in a staff capacity directly under the Executive Director. These are the Special Projects Office, the University Participation Office and the Fellowship Office.

The Special Projects Office is chiefly responsible for the development of domestic conferences, symposia and special institutes. The University Participation Office administers the series of programs primarily designed to take advantage of the unique research facilities at the U. S. Atomic Energy Commission installations at Oak Ridge, the Savannah River Laboratory and the Puerto Rico Nuclear Center for the advancement of nuclear science and education. These include the Faculty Participation, Atomic Energy Commission Postdoctoral Fellowship, Oak Ridge Graduate Fellowship, Traveling Lecture and Student Trainee programs. The Fellowship Office is responsible for administration of the AEC special fellowships in nuclear science and engineering, health physics and advanced health physics.

The teacher-training program formerly administered by the University Relations Division was transferred to the ORINS Special Training Division.

Now, the institution originally organized to aid Southern scientists enters upon its third decade, with a new corporate entity, and the change is already being reflected in the scope of its activities outside the field of nuclear energy. While the U. S. Atomic Energy Commission still remains as the principal source of funds for the activities of the Oak Ridge Institute of Nuclear Studies, it is both surprising and heartening to realize that, in the past fiscal year alone, O.R.A.U., under interagency agreements, has undertaken nonnuclear projects amounting to almost $500,000 for the Tennessee Valley Authority, the Economic Development Administration, the U. S. Office of Education, the U. S. Department of Labor, the National Aeronautics and Space Administration, the Office of Economic Opportunity and the U. S. Army Medical Research and Development Command. In addition, grants totaling almost $135,000 have been received from the National Institutes of Health and the National Science Foundation for medical research and in-service institutes for elementary and secondary school science teachers.

The accompanying report, detailing the activities of Oak Ridge Associated Universities for the fiscal year July 1965-June 1966, is an eloquent delineation of the great—almost fantastic—progress of an institution that originated in "a chance remark" at a faculty party. It is our sincere hope that these twenty years of growth are but the opening chapters of a long and happy story.

Medical Division

Considerable growth and development highlighted the program of the Division, which conducts its clinical and laboratory research programs in one of the major "on-site" biomedical laboratories supported by the U. S. Atomic Energy Commission.

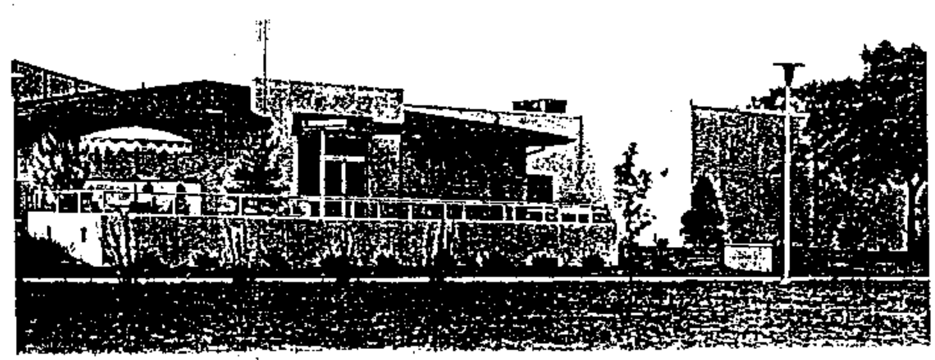
The primary mission of the Division is to obtain new information on radiation effects and to advance beneficial medical applications of radioactivity. Allied programs include an investigation of human responses to irradiation, conducted for the National Aeronautics and Space Administration. A growing primate program, based on the special features of a small marmoset, *Tamarinus nigricollis*, is supported principally by a grant from the National Institutes of Health.

The special facilities of the Division provide unique opportunities for studies of total-body irradiation and for the measurement of whole-body radioactivity over a wide range of sensitivities. In addition, the 34-bed hospital unit and related laboratories offer appropriate space and equipment for patient care and research, as well as for animal experimentation and a variety of other biological investigations.

Among the significant events of the year was the construction of the new low-dose-rate irradiation facility, which is scheduled for completion in the summer of 1966. It is expected that the facility will be fully operational later in the year.

An increasing number of scientific papers and publications by staff

This view of the patient wing of the Medical Division shows the heavily-shielded roof of the low-level whole-body counter (left foreground). The new low-dose-rate human irradiation facility (at right) is nearing completion, and will be used to treat leukemic patients with prolonged therapy schedules.



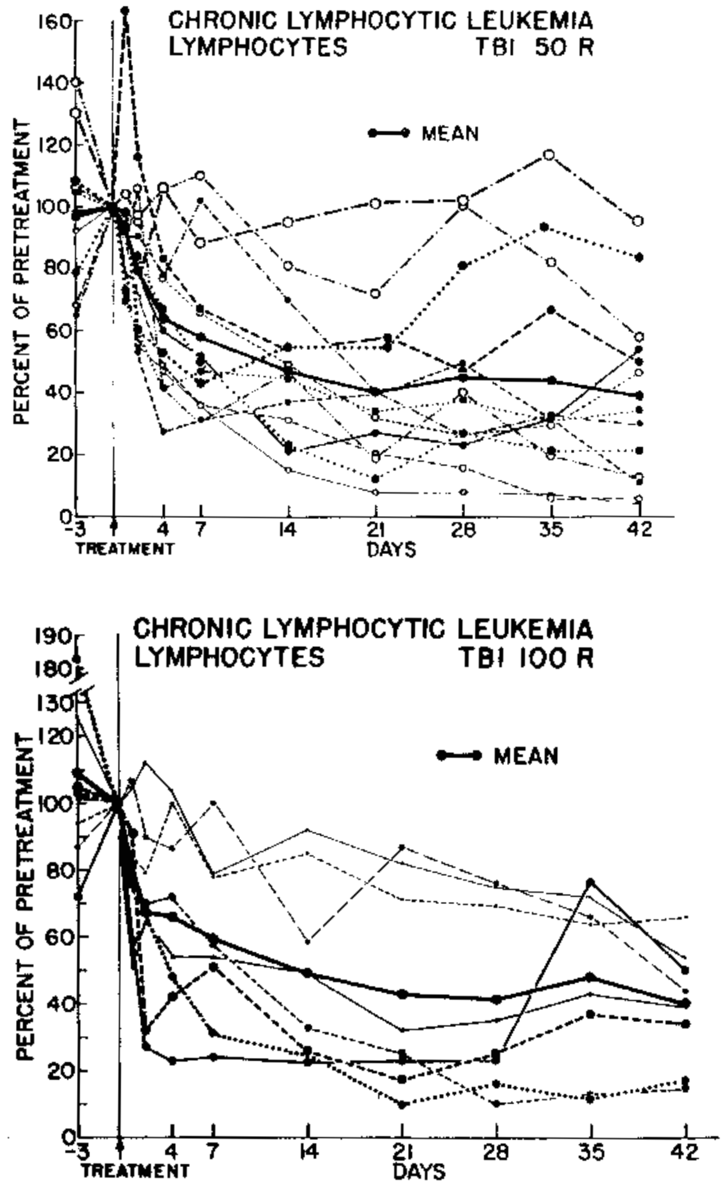
members of the Division is evidence of the continuing productivity of the research program. Staff members have also participated in the programs of major national and international scientific meetings. Gould A. Andrews, Division Chairman, presented a paper on *The Effects of Various Types of Ionizing Radiations from Different Sources on the Haematopoietic Tissue* at an International Atomic Energy Agency-sponsored conference in Vienna, Austria. Nazareth Gengozian and Arthur Kretchmar each presented papers at the International Congress of Radiation Research in Cortina, Italy.

Radioactive Pharmaceuticals was the topic of the 9th Symposium in Medicine held November 1-4, 1965, sponsored by the Division. Some 40 guest lecturers from the United States and abroad assembled for the purpose of summarizing and correlating recent advances in the development of radioactive pharmaceuticals for use in clinical medicine and biological research. The proceedings were published under the title *Radioactive Pharmaceuticals*, by the Atomic Energy Commission's Division of Technical Information Extension, edited by Gould A. Andrews and Ralph Kniseley of O.R.A.U. and Henry N. Wagner, Jr., Johns Hopkins University; Elizabeth Anderson of O.R.A.U. was technical editor. Plans are now being completed for the 1966 symposium on *Compartments, Pools, and Spaces in Medical Physiology*, scheduled for October 24-27, in Oak Ridge. These proceedings will also be published as part of the Atomic Energy Commission Symposium Series.

Several staff changes occurred during the year. Late in 1965, Granvil Kyker, for many years a research scientist at the Medical Division, was appointed Head of the Fellowship Office of Oak Ridge Associated Universities. Randall Wood, previously assigned to the lipid program as a postdoctoral fellow, joined the regular scientific staff.

Mechanisms of Radiation Injury and Treatment

Total-body irradiation continued to be important in the treatment of chronic leukemias, polycythemia vera, and lymphosarcoma. The effects of various doses of irradiation on the blood cells and bone marrow have been analyzed to determine the extent to which the state of the patient and his disease may influence his response to radiation. In patients with chronic leukemia, the white blood cell levels appear more sensitive to radiation than in those without the disease. Observations on total-body irradiation in these patients with blood diseases might appear to be of more value in studying the disease than in predicting radiation responses of normal persons; but these investigations are applicable to such radiobiological problems as accidental exposure in industry, military applications, and space exploration because they define a maximum sensitivity of the human organism.



Plot of lymphocyte values in two groups of patients treated with total-body irradiation. The group receiving 50 R and the group receiving 100 R both show wide individual variations in response, but the mean values for both groups are similar. This material is part of the Division's program analyzing the effects of total-body irradiation in patients with leukemia and other malignant disease.

One important effect of radiation on animals is the development of a large increase in the number of fat cells that contain triglycerides in the bone marrow during the first few days after irradiation, at a time when the blood-forming elements are decreased. This change is produced only in the marrow directly in the radiation beam, and investigations are clarifying the biochemical mechanisms associated with fat-cell formation; there is severe inhibition of the oxidation of fatty acids, the biosynthesis of phospholipids, and the turnover of triglycerides. The data imply that the enzymes or the cells that synthesize triglyceride are more resistant to ionizing radiation than those that synthesize phospholipid.

Recently, Division staff members designed a model that helps to clarify the relationships of lipid metabolism in normal and irradiated bone-marrow cells. Normally there is an intermediate metabolic pathway for synthesis of triglycerides and phospholipids from diglycerides; such a pathway was previously known to exist in the liver. The block in phospholipid synthesis and concomitant increase in the triglyceride pool of irradiated marrow suggest the presence in the diglyceride pathway of a control mechanism for fat-cell production. This project has developed a framework of ideas for establishing the complex relationships that exist in the bone marrow between the cellular lipids and the blood-cell forming activity. The findings also are applicable to the broader problem of derangements in hemopoiesis that occur in disease and radiation injury.

A second significant finding has been made in the study of the intermediary metabolism of the glyceryl ethers, which are normally found in bone-marrow cells and thought to contain intrinsic hemopoietic and radioprotective capabilities. The demonstration that the liver is capable of causing complete cleavage of the glyceryl ether bond indicates that any biological activities thought to be inherent in glyceryl ethers should not be attributed to the intact compounds and must reside in one or more of their metabolic products. Thus current studies are directed toward the effects of these metabolic products on functioning hemopoietic tissue.

Important related work in the study of the ether-containing lipids has revealed an unidentified lipid class containing some glyceryl ether diesters to be prevalent in tumors (rat, mouse, human) but not in normal tissues or fluid supporting the growth of tumor cells.

Studies in the immunology program have revealed an abnormality in the process of antibody formation in chimeric mice, animals that have been irradiated and protected from death by the injection of bone-marrow cells from healthy mice of a different strain. The protected animals are "chimeric" in that they have two genetic types of tissue, their own and the transplanted

marrow. Such animals are likely to suffer from secondary or homologous disease, a wasting disorder that is due to lack of compatibility between the two types of tissue. Information relating to the immune systems of such animals is important in explaining this disorder, and may have broad applications in human tissue transplantation.

Recent studies show that the protected animals do not respond normally to the injection of an antigen such as typhoid vaccine; that is, they do not develop immunity in the normal fashion. Normal mammals respond to the vaccine by producing predominantly a large antibody (19 S macroglobulins) during the first two weeks and then, during subsequent weeks, mainly a smaller (7 S gamma-globulin) antibody. The mice with the marrow transplant showed a pronounced reduction in formation of the second, smaller type of antibody. This abnormal pattern was accentuated when repeated injections of antigen were given. This work is expected to cast additional light on the immune mechanisms involved in marrow transplantation and secondary disease. The finding also provides a valuable model for the study of the physiology of antibody formation in the mammal.

Previous Division research has shown that the success of transplantation of rat bone marrow in irradiated mice is dependent upon the rate at which the radiation exposure was given. More recent studies were designed to investigate whether a similar phenomenon occurs at a higher total dose of radiation (900 to 1200 R), and when the transplantation is of homologous bone marrow; that is, marrow from mice of an unrelated strain. Of the mice receiving 900 R and homologous marrow, the survival rate was increased only in those receiving a relatively high exposure rate (39.7 R/min and 53.4 R/min). However, a donor graft could not be detected in the 30-day survivors of mice in any of the four exposure rates used.

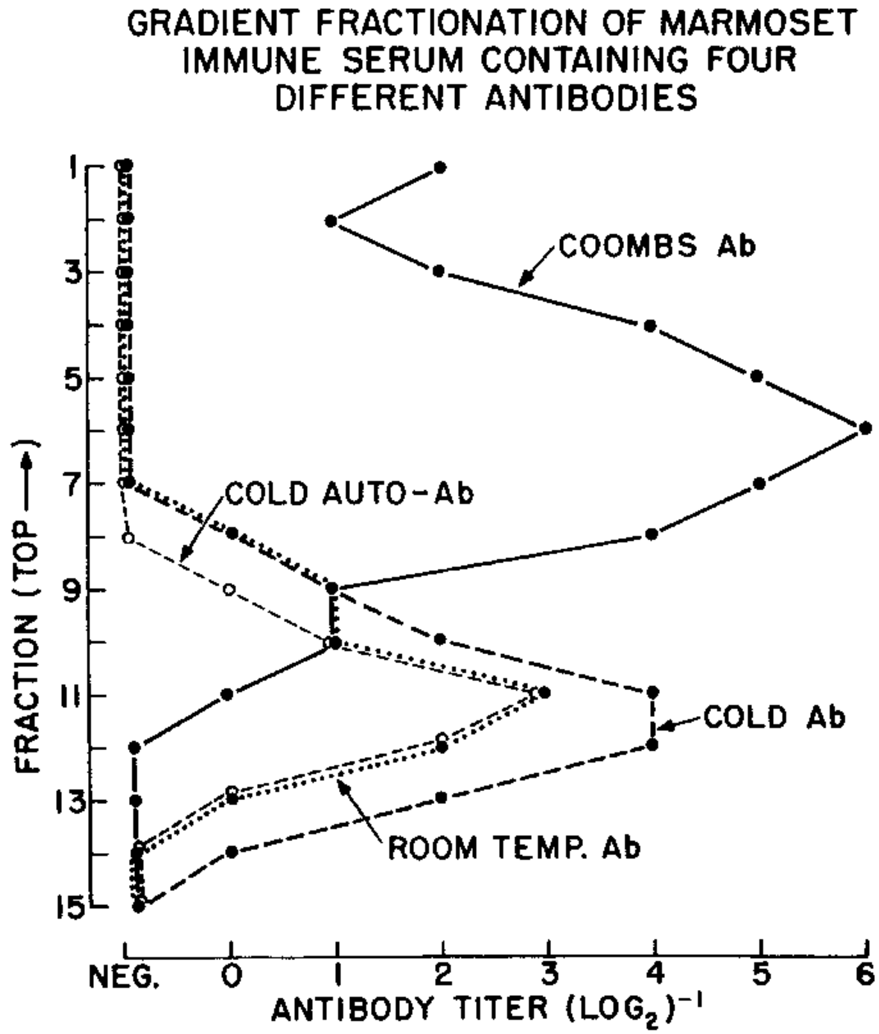
Of the mice receiving 1200 R and homologous marrow, increased survival rates were obtained for all three different exposure rates studied (3.75 R/min, 39.7 R/min, and 53.4 R/min). However, only in the two higher dose-rate groups was a permanent transplant of marrow effected. It is apparent that the effect of the homologous marrow at the lower exposure rate was to provide a protection from hematopoietic death until the animal's own hematopoietic system recovered from the radiation damage.

An analog computer has been used to create models (statistical representations) that will simulate the recovery of the bone marrow in mammals after total-body irradiation. The model predicted that after irradiation and injection of bone marrow in experimental animals, complete recovery could occur in the peripheral red blood cell levels without corresponding complete recovery in the stem-cell pool. This prediction was then tested in animal experiments, and was verified. Irradiated mice given injections of bone-marrow cells do not completely regenerate their marrow cell populations, even though they may show complete recovery to normal values in hematocrit, hemoglobin, reticulocyte, and serum levels. This was true when the irradiated mice were given isologous bone marrow (marrow from genetically identical donors) and when they were given homologous donor bone marrow (marrow from mice of a different genetic strain). Also, it was found that an additional delayed reduction in the size of the stem-cell pool occurred 20 to 40 days after irradiation in animals that had been saved from death by a bone-marrow graft from another genetic strain. Approximately 200 days are required for mice carrying a foreign graft to achieve a bone-marrow cell population with the same capacity to produce red cells as is seen in mice given isologous marrow. The recovery in mice given isologous cells is rapid, but is not up to that of normal controls even at 132 days after irradiation.

Examinations are in progress on the chromosomes of patients who have been treated with radiation, and on men who were exposed in a radiation incident in 1958. A new observation was made recently in the latter group. In addition to breakages in chromosomes, a previously observed change, an abnormally small "G" group chromosome was discovered, which resembles the so-called *Philadelphia* chromosome seen in patients with chronic granulocytic leukemia. The abnormal form has been thought to be due to a deletion of one of the long arms of a "G" chromosome, and the present result leads to speculation that the *Philadelphia* chromosome might be analogously the result of a chromosomal or chromatid break. In spite of the resemblance of this small chromosome to the abnormal chromosome of granulocytic leukemia, the three men who have it show no evidence of having leukemia, and thus this smaller "G" chromosome probably does not have the same significance as the *Philadelphia* chromosome. Moreover, these men have a much lower incidence of the abnormal chromosomes than is found in patients with chronic granulocytic leukemia.

Experimental Studies on a Small South American Primate

Considerable success has been achieved in developing the marmoset colony. Immunologic studies are especially interesting because birth of fraternal twins is an almost consistent occurrence, and is accompanied by blood chimerism of the young. Experimental results indicate the existence of major antigenic blood groups among the marmosets and show the feasibility of obtaining reagents capable of delineating animals by their red cell antigens. One experiment under way uses assay of the degree of chimerism to select "low-level chimeras," which would be ideal for immunization to



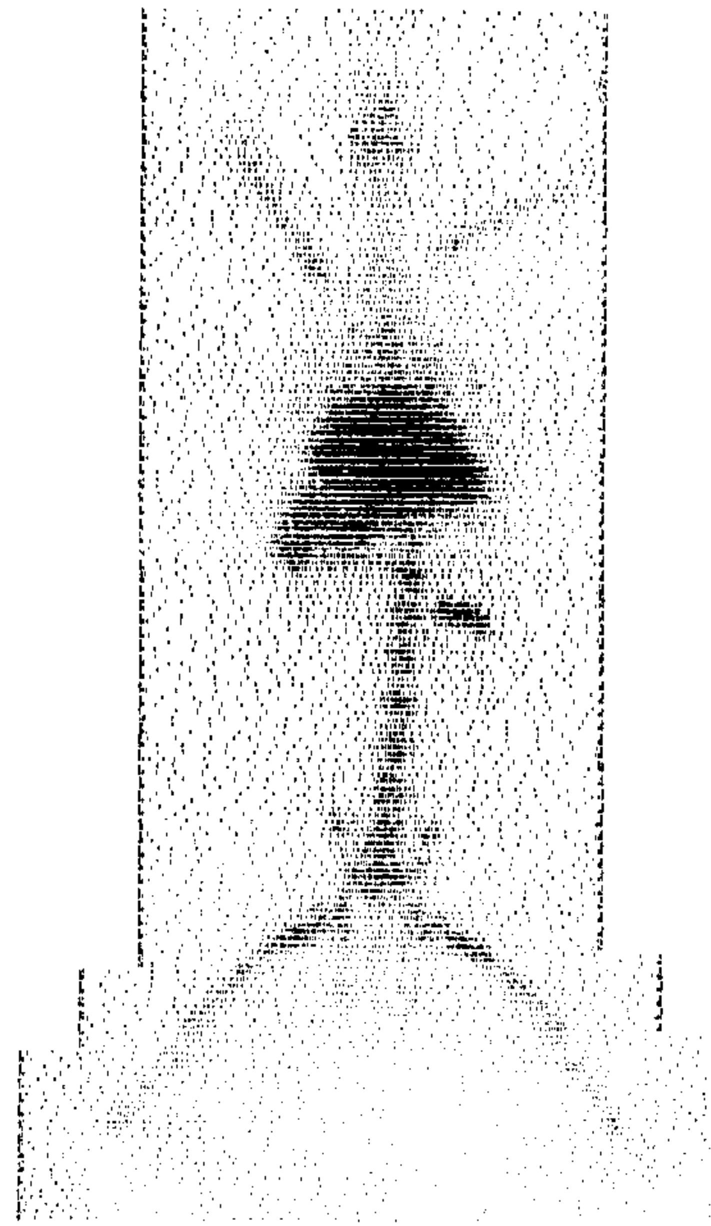
Isoimmunization of a marmoset with red blood cells of another marmoset resulted in the formation of four qualitatively different antibodies: (a) an incomplete isoagglutinin of small molecular weight detectable by a Coombs test; (b) a large molecular weight antibody reactive at room temperature; (c) a cold isoagglutinin of large molecular weight; and (d) a cold autoagglutinin (reactive with cells of the immunized recipient) of large molecular weight. These are illustrated in a gradient sedimentation curve, the large antibodies being found in the lower fractions of the gradient and the light, incomplete antibody located in the upper fractions.

produce blood-typing reagents. Tests thus far for naturally occurring isohemagglutinins have been negative.

Although breeding of this marmoset has been successful, a significant fraction of the pregnancies has terminated in spontaneous abortions, stillbirths and premature deliveries. Pathologic studies of a recent stillborn foetus and its twin that lived for 16 days suggested that a disease similar to erythroblastosis foetalis was present in both. Similar evidence of the disease was obtained in twins that died near term *in utero* after the traumatic death of their mother. The natural occurrence of hemolytic disease of the newborn in this species is of particular interest in view of the nature of the twinning. The marmoset, therefore, appears to offer experimental approaches to the study of the prevention and cure of this disease. Also, one obvious way to promote a successful breeding program would be the selection of suitable male-female pairings for mating. Findings in over 500 necropsies have been catalogued and are being reported. The most serious pathogens of imported specimens are parasites, especially an intestinal parasitic worm, an acanthocephalan of the genus *Prosthenorchis*.

Medical Radioisotope Development

During recent months work with gallium-68 has progressed rapidly, and this radionuclide has shown great promise as a practical diagnostic agent. It appears that, in different chemical forms, it may prove useful for several unrelated diagnostic applications. The studies have been mainly on its deposition in bone, where it is particularly useful for the early diagnosis of metastatic bone tumors. Work on a colloidal form for studies of the reticuloendothelial system also has been initiated. Gallium-68 has several properties that recommend it as a diagnostic agent. It has a short half-life, decays by positron emission, and is obtained as the daughter of a long-lived parent radionuclide (^{68}Ge). Thus a generator, or "cow," once filled with the parent nuclide will provide a hospital with ^{68}Ga for many months. As demonstrated in past work with ^{67}Ga, the amount of stable carrier administered has a pronounced effect on tissue distribution of ^{68}Ga. As the dose administered approaches the carrier-free level, the distribution becomes diffuse. With sufficient carrier gallium, the ratio of bone to blood and bone to muscle approaches 25:1 and 100:1. The amount deposited in the bone increases to a maximum value at about one hour after administration. Gallium-68 in the EDTA form is rapidly excreted, and deposition in the bone and tissues, other than the kidneys and urinary bladder, is insignificant.



Scan of rabbit showing uptakes of ferric oxide colloid labeled with radioactive gallium (^{68}Ga). As part of the program of medical radioisotope development, experiments are in progress attempting to increase the percentage of localization in marrow.

The amount found in the kidney has led to an investigation of this nuclide as a diagnostic agent for detection of kidney disease.

Colloidal hydrous ferric oxide combined with ^{68}Ga is being developed as an agent for scanning the reticuloendothelial system. Initial tests in animals have given encouraging results, and the preparation may have value for scanning liver, spleen, and, especially, bone marrow. The use of other radionuclides in this chemical form is being investigated, since the technique may have several applications.

Radioisotopes in Diagnosis

New emphasis is currently being placed on theoretical and mathematical approaches in the use of radioisotopes in diagnosis, detection and evaluation of tumors.

Gallium-68 as the citrate has been used in skeletal scans of patients with known or suspected bone lesions. As with other bone-scanning agents, it has been possible to demonstrate cancer that has spread to bones before the lesions are visible on X-rays. When bone metastases are detected, the tumor therapy may be significantly altered. Palliation of the pain can often be achieved with localized irradiation.

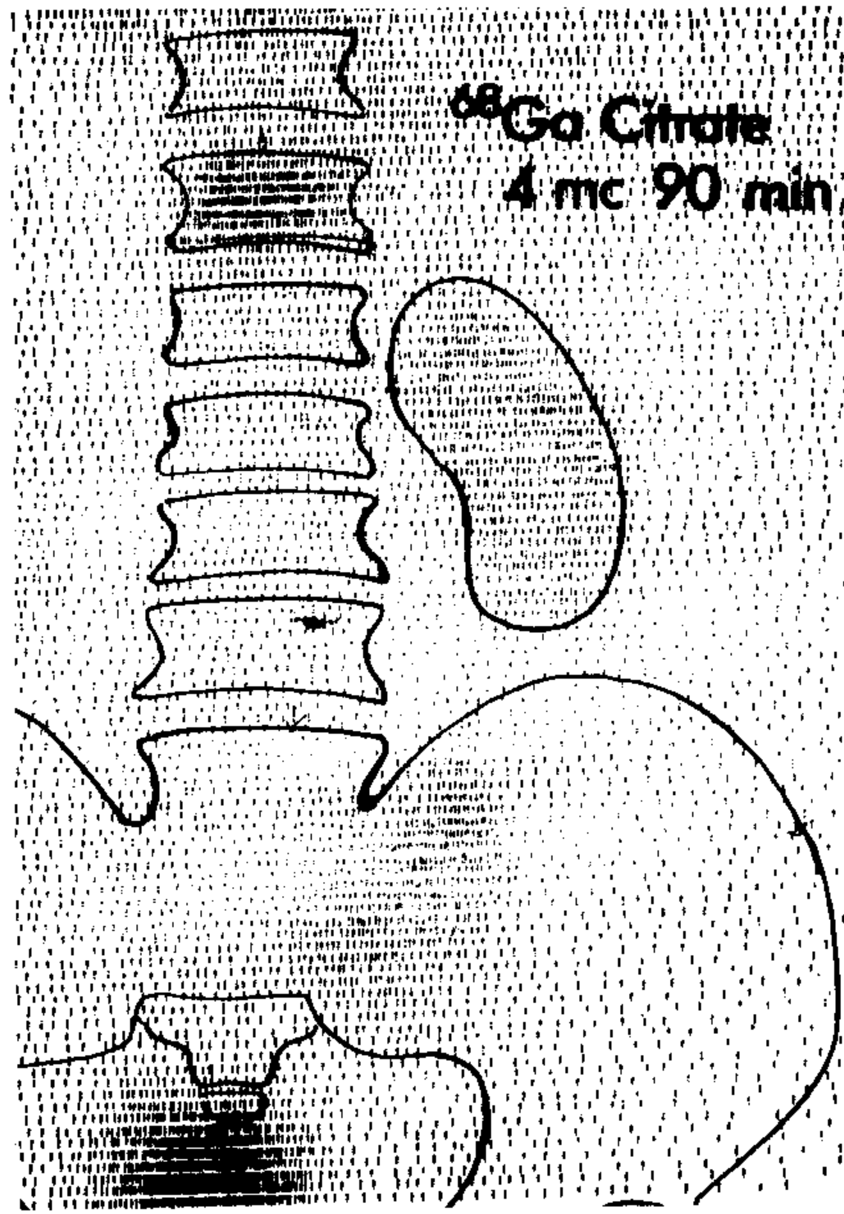
The study of the distribution of functioning bone marrow in patients with a variety of disorders affecting the blood-forming organ has shown further progress. The whole-body scanner has proved to be a useful tool in this work. Responses to destruction of marrow, the patterns of extension of the active marrow into the extremities, the sites and shape of local lesions, and the hyperplasia in some anemias can be shown.

To produce better bone-marrow scans, improved radioactive colloids are needed. One of the main requirements is to reduce the radiation dose to the patient so that the diagnostic test can be performed without concern, even in patients without serious disease. Clinical trials have begun with colloidal preparations of ^{99m}Tc and ^{159}Gd, since they offer some advantages. More recently, ^{68}Ga-labeled colloidal ferric oxide has been given pilot trials.

Instrumentation problems for bone-marrow scanning are more complex than for any other organ scanning, especially because of the variable depth of the marrow from the surface of the body. In spite of difficulties, scans of good quality have been produced.

Therapy with Radiation

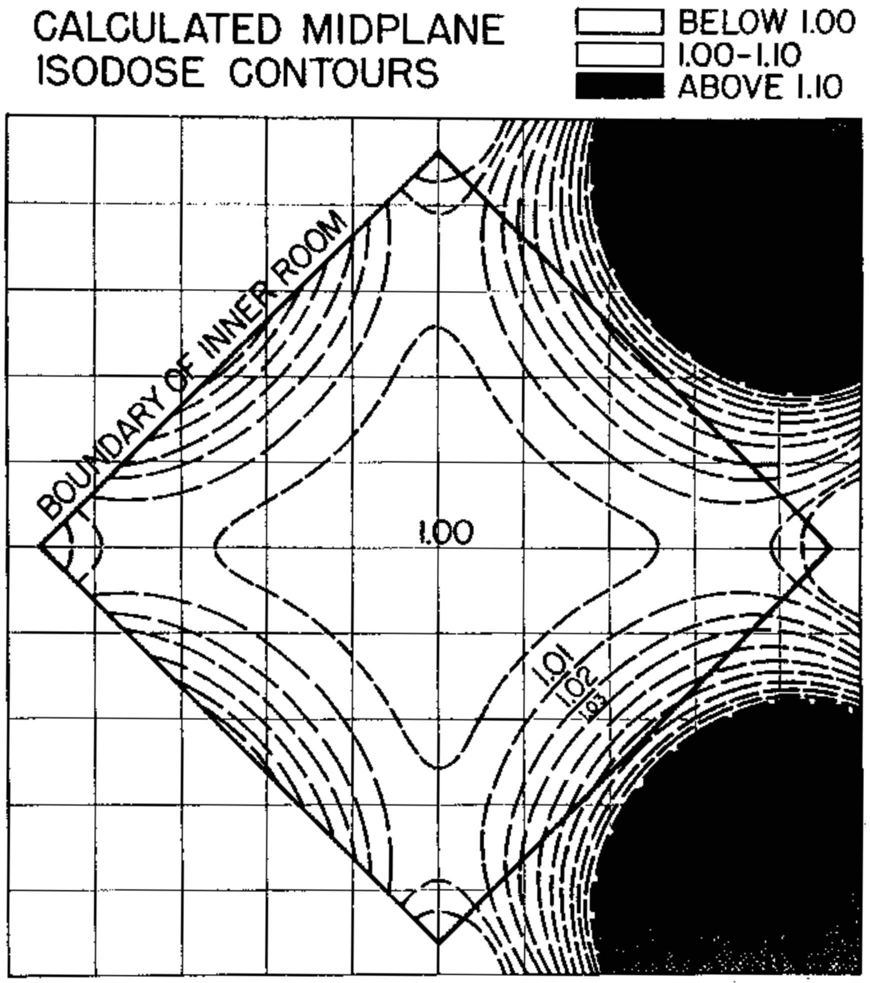
An important objective always has been to develop and assess improved methods of therapy with radiation, both internal and external. By continuing efforts to obtain best selection of patients, radiation dose and dose rate, it is hoped to improve the usefulness of total-body irradiation. Uniform proto-



Scan of a 78-year-old patient with cancer of the prostate gland taken 90 minutes after injection of 4 millicuries of gallium-68 citrate. Bone scans revealed sites of metastic cancer involving the spine and pelvis. Neither of these lesions could be seen initially on X-ray studies. The use of radioactive gallium as an agent for bone scanning is one of the current clinical projects at the Division.

LOW-DOSE-RATE HUMAN IRRADIATOR

CALCULATED MIDPLANE ISODOSE CONTOURS



This diagram shows the calculated dose rates at midplane in different parts of the low-dose-rate human irradiator now nearing completion at the Division. Less than 10 per cent variation in exposure rate was one of the design requirements in planning the facility. The project is sponsored jointly by the Atomic Energy Commission and the National Aeronautics and Space Administration. Patients with leukemia will be given prolonged treatments and, during these periods, will be housed in a comfortably furnished room which allows free movement.

cols have been established so that careful assessments of patients can be carried out through an adequate follow-up period.

The use of lower exposures (50 to 100 R) has been continued, principally in patients with chronic leukemia and lymphoma. In addition to furnishing valuable information to staff scientists about the response of the disease by this treatment, these investigations have provided data needed by the Atomic Energy Commission and the National Aeronautics and Space Administration on radiation effects in man. Among the patients with lymphoma or chronic leukemia given relatively low doses, few fail to show improvement, although the response does vary. As might be expected, additional therapy is required with the passage of time, either in the form of repeat total-body irradiation, ^{32}P, chemotherapy, corticosteroids, or local radiotherapy. In general the benefits of low-dosage total-body irradiation appear to be comparable to conventional forms of systemic therapy for these diseases.

Experience with polycythemia vera has included six patients who have received 100 R. A preliminary impression is that 5 millicuries of ^{32}P treatment may have a greater and more prolonged therapeutic effect than 100 R total-body irradiation in patients with this disease.

The retrospective study on radiosensitivity in man continues to be a significant area of Division research. More accurate dose-response relationships are needed for man before the success or failure of a space flight through a radiation field can be predicted on the basis of radiobiologic probability equations. At present, it is not known whether the prodromal radiation syndrome—nausea, loss of appetite, vomiting, diarrhea, apathy and increased fatigability—would lead to delayed or lowered performance capabilities, but it seems justified to assume that it would. For this reason emphasis is placed on determining the radiation dose-response relationships for these six most common symptoms of the prodromal radiation syndrome. No dose-correction factor for converting this information from sick to well man is now available, but it is believed that the bias caused by disease can be minimized by expansion of these studies to include the data of other investigators who gave total-body irradiation to patients with nonhematologic diseases, and a number of other institutions are collaborating in supplying data from their own therapeutic total-body irradiation patients.

Plans are under way for the collection of new information on radiation exposure, and to this end the construction of a new low-dose-rate irradiation facility is in process supported jointly by the National Aeronautics and Space Administration and the Atomic Energy Commission.

This facility, designed to treat patients with leukemia and other malignant diseases by exposing them to prolonged exposures at dose rates of

1 R/hr., will include a comfortable living area about 14 x 14 feet. During treatment, electronic monitoring apparatus will be used to collect information on physiological responses that will be useful to the National Aeronautics and Space Administration.

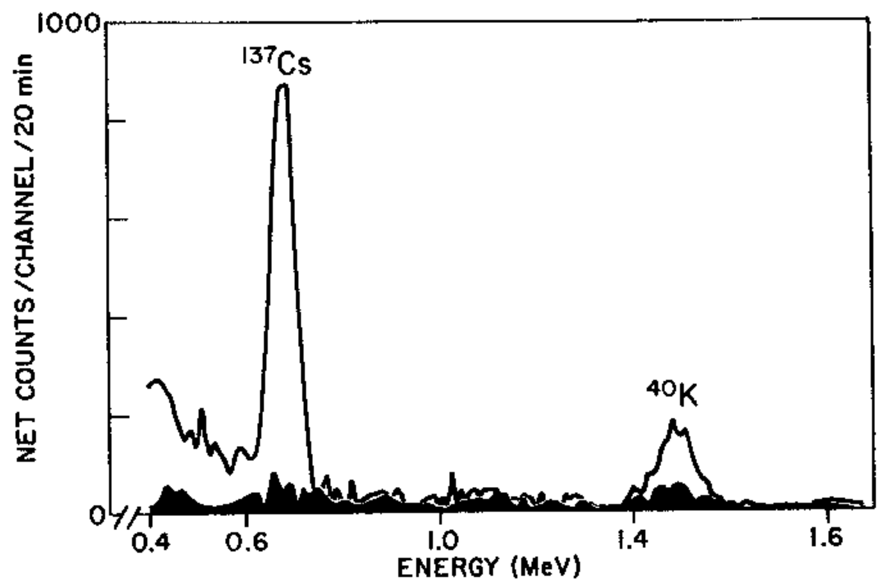
Theoretical Biology

Efforts continued to examine theoretical concepts on which a number of biomedical studies are based. The tracer system approach itself has been studied, comparing the classic closed and open systems, and conclusions were reached that may invalidate earlier methods. The concept of exchangeable mass has been reevaluated and equations have been developed for studies of potassium and sodium metabolism that can be applied in man, using whole-body counting techniques. In another area, the red cell survival data were subjected to scrutiny and a formal model for the normal systems was formulated. Nonstationary (non-normal) systems were studied in terms of perturbations of the normal. In connection with this problem, DF^{32}P (radioactive di-isopropyl-fluorophosphonate) data have been used, and a mathematical description of the discrepancy between whole-body and peripheral blood retention of ^{51}Cr-labeled red cells was devised.

Instrumentation Development and Methodology

The medium-level whole-body counter, designed to measure gamma-emitting radionuclides, has been evaluated clinically by studying patients receiving diagnostic doses of ^{131}I. Confirmed in these patients was the finding that the spectral changes produced by movement of the radioisotope in the body are minimized if the counting rates are taken at a carefully selected scatter-energy range, rather than at peak energies. When retention measured on the whole-body counter is compared with thyroid uptake, we find a better correlation than when we make a similar comparison using retention as computed from urine and fecal excretion data.

The low-level whole-body counter was used to measure activity in numerous normal and ill persons. Retention studies have been started with ^{140}La, ^{47}Ca, ^{28}Mg, ^{99m}Tc, ^{68}Ga, ^{131}I, ^{159}Gd, ^{198}Au, ^{51}Cr, ^{60}Co, ^{160}Tb, and ^{22}Na. The absolute efficiency of the counter is being determined in cooperation with the Atomic Energy Commission Committee for Whole-Body Counter Calibration. This will provide worldwide cross reference for future measurement. Such studies on the performance of the counter have necessarily preceded the complete development of a research program. We are

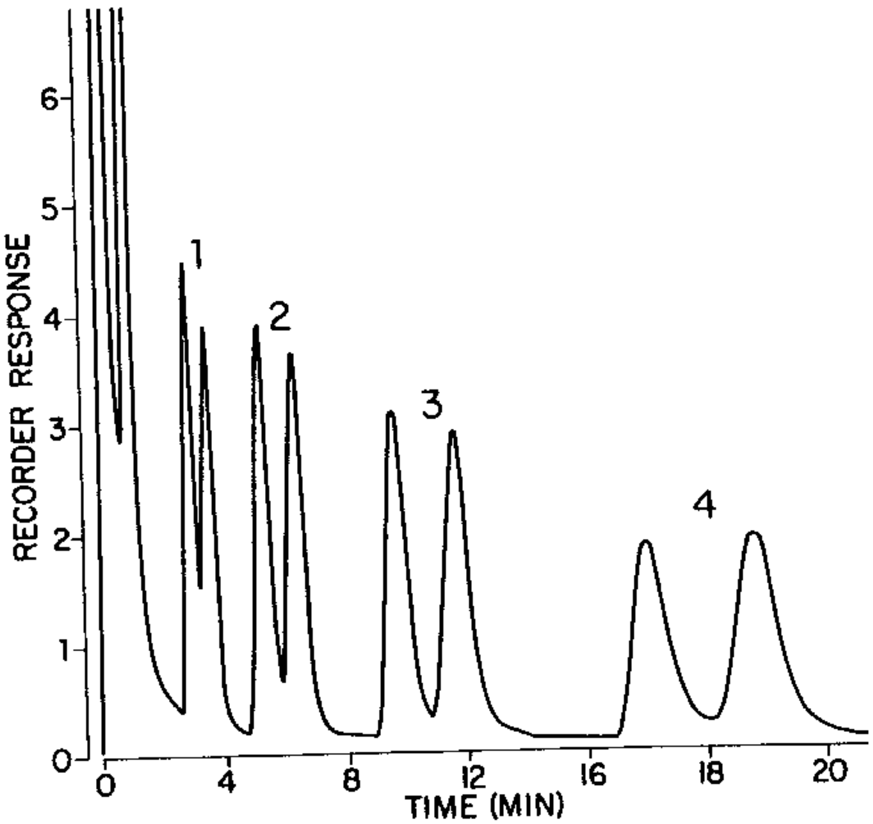


Among the interesting spectra of patients with complicated problems being studied by whole-body counting, several stand out because of their implications for research. Shown are spectra from one such patient compared with a normal person. The patient, suffering from a serious metabolic disturbance involving principally electrolyte balance, was found to have abnormally low cesium-137 and potassium-40. The normal subject contains spectral peaks for these two radionuclides that are almost absent in the patient.

concerned with the effects of body size and distribution of the isotope and with factors influencing background counting rates.

An electronic method was developed for measuring red blood-cell fragility and it can be used for rapid screening of large numbers of blood samples for detection of red cell abnormalities as reflected in altered osmotic fragility. The application of the instrument to measuring red cell sensitivities to saponin, venoms and other hemolytic agents is in progress.

Methodologic improvements related to the lipid program included a quantitative method for gas chromatograhic analysis of isomeric glyceryl ethers; a modification of an applicator for use in thin-layer chromatography for more accurate photometric analysis; and a comparison study of zonal scans, strip scans and autoradiographic scans of thin-layer chromatograms which demonstrated the superiority of zonal scans in terms of sensitivity and preparation time.



One of the recent significant analytical advances at the Division has been the development of a gas-liquid chromatographic procedure (Lipids 1,62,1966) for the separation of glyceryl ether isomers (as their trifluoroacetate derivates) that are found in complex biological mixtures. Quantitative resolution of these isomers previously was impossible. Biological studies of the glyceryl ethers at the Division concern their intermediary metabolism and their function in tumor and hemopoietic cells.

TRAINEES IN CLINICAL INVESTIGATION

Jaime J. Ahumada–Colombia
Masayuki Takasugi–Japan
B. V. Suryanarayana–India

JAMES PICKER FOUNDATION FELLOW

Noboru Arimizu–Japan

DAMON RUNYON FOUNDATION FELLOW

Yasuhiko Ito–Japan

ABBOTT STUDENT FELLOWS IN NUCLEAR MEDICINE

Karen Fu–College of Physicians and Surgeons, Columbia University, New York
William Kean–Meharry Medical College, Nashville, Tenn.
Thomas Logan–Meharry Medical College, Nashville, Tenn.
Landrum Tucker–Stanford University School of Medicine, Stanford, Calif.

RESIDENT PHYSICIANS

Joseph Ferrucci–Massachusetts General Hospital, Boston
Donald Fleischli–Massachusetts General Hospital, Boston
Bruce Haskin–Massachusetts General Hospital, Boston
Gerald Kolodny–Massachusetts General Hospital, Boston
Milton Weiner–Massachusetts General Hospital, Boston
George Zinninger–Massachusetts General Hospital, Boston

VISITING SCIENTIFIC GUESTS

James Lim–University of North Carolina, Chapel Hill

MEDICAL DIVISION CONFERENCES–1965

July 1: An instrument for measuring red cell fragility–A. C. Morris and C. C. Lushbaugh, Division staff.

July 8: Theoretical and practical aspects of DFP^{32}-labeled RBC life span studies–Douglas Lawson and Walter L. Scott.

July 15: Cytogenetic studies in acute leukemia—Kong-oo Goh, Division staff.

July 22: A method for determining changes in psychiatric status due to physiologic and environmental changes—Louis A. Gottshalk, department of psychiatry, University of Cincinnati.

July 29: Cholesterol flux in rabbit atherosclerotic lesions—Howard I. Newman, University of Tennessee department of physiology, Memphis.

August 5: Myelocyte division—Helen Vodopick, Division staff.

August 12: Enzyme studies in myeloproliferative diseases—Francis Goswitz, Special Training Division staff.

August 19: The rapid incorporation of dietary linoleic acid into triglycerides of irradiated bone marrow—J. N. Bollinger, Division staff.

August 26: Thyroid scanning—experience with 340 patients in Bogota, Colombia—Efraim Otero-Ruiz, Instituto Nacional de Cancerologia, Bogota, Colombia.

September 2: Bone scanning with gallium-68—Jaime Ahumada, Instituto Nacional de Cancerologia, Bogota, Colombia.

September 9: Research activities of summer students—N. Gengozian, Division staff.

September 16: Autoradiographic cytogenetics—Kong-oo Goh, Division staff.

September 23: Basic studies of gallium distribution—Ray L. Hayes, Division staff.

September 30: Biochemical and clinical studies of lactate dehydrogenase—Virginia Holten, Division staff.

October 7: Changes in bone marrow radiosensitivity, under vascular hypoxia, as measured by spleen colonies in mice—F. Comas, Division staff.

October 14: Erythropoietic capacity of radiation chimeras—A. L. Kretchmar, Division staff.

October 21: Some inorganic colloids in biological systems—Granvil C. Kyker, O.R.A.U. staff.

October 28: Review of the ORINS lipid program—Fred Snyder, Division staff.

November 11: Oxygen and radiosensitivity—F. Comas, Division staff.

November 15: Changes induced in the first post-irradiation generation cycle of cells in tissue culture—Otto Vos, Medisch Biologisch Laboratorium, Rijswijk, Belgium.

November 18: Iron metabolism—too much or too little—Matthew Block, professor of medicine, University of Colorado Medical Center.

November 19: Biochemical basis for red cell morphology—Matthew Block, professor of medicine, University of Colorado Medical Center.

December 2: Lipid patterns of human tissues—Helmut Mangold, University of Minnesota.

December 9: Evaluation of the thyroid nodule—Soloman Silver, Mt. Sinai Hospital, Columbia University College of Physicians and Surgeons, New York, N. Y.

December 16: Maturation of rat megakaryocytes studied by microspectrophotometric measurement of DNA—Theodore T. Odell, Biology Division, Oak Ridge National Laboratory.

December 23: The metabolism of the alpha alkoxy glyceryl ethers—Raymond C. Pfleger, Division staff.

December 30: The distribution of "red" and "yellow" marrow in humans, as determined at autopsy—Bill Nelson, Division staff.

MEDICAL DIVISION CONFERENCES—1966

January 6: Mathematical descriptions of the consequences of radiation dose protraction—HAL HOLLISTER, chief of technical analysis branch, Division of Biology and Medicine, Atomic Energy Commission, Washington, D. C.

January 13: Chromosome studies in malignant lymphomas—A. G. BAIKIE, University of Melbourne, Victoria, Australia.

January 20: Radiation-induced chromosomal aberrations in man—MARCO STEINMAN, research assistant, cytogenetics, Division staff.

January 27: Lipids and the blood cells—FRANK GOSWITZ, Special Training Division staff.

February 3: Gallium-68 scanning of the reticuloendothelial system—RAY HAYES, Division staff.

February 10: Mode of action of erythropoietin—ARTHUR L. KRETCHMAR, Division staff.

February 17: Report of the Atomic Energy Commission Biomedical Directors' meeting—RALPH M. KNISELEY, Division staff.

February 24: Clinical applications of the scintillation camera—A. GOTTSCHALK, University of Chicago, department of radiology.

March 10: Current work at Oak Ridge National Laboratory in nuclear medical instrumentation—C. CRAIG HARRIS, Oak Ridge National Laboratory.

March 17: The GLC and TLC resolution of diastereoisomeric polyhydroxystearates and assignment of configurations—RANDALL WOOD, Division staff.

March 24: Clinical iron absorption—MASAYUKI TAKASUGI, Division staff.

March 31: Histocompatibility testing—HELEN VODOPICK, Division staff.

April 7: A lipid found exclusively in tumors—FRED SNYDER, Division staff.

April 14: Intermittent corticosteroid therapy in the malignant lymphocytic diseases—DAVID A. WHITE, Division staff.

April 21: The computer program for the Medical Division—ARTHUR S. GLOSTER and FRED BROWN, O.R.A.U. staff.

April 28: Models and representations: exchangeable mass—PER-ERIK BERGNER, Division staff.

May 5: The metabolic fate of ether-containing lipids—RAYMOND C. PFLEGER, Division staff.

May 12: Irradiation of liver and spleen in chronic myeloid leukemia—F. COMAS, Division staff.

May 19: Comparison of gamma ray and neutron exposures of large animals—D. G. BROWN, University of Tennessee Agricultural Research Laboratory.

May 25: Metabolic interrelationships of polyunsaturated fatty acids—R. R. BRENNER, National University of La Plata, Argentina.

May 26: Bone scanning with gallium-68 citrate—C. LOWELL EDWARDS, Division staff.

June 2: Immunologic studies in the marmoset—N. GENGOZIAN, Division staff.

June 9: Clinical evaluation of anemic patients using radioisotopes—FRANCIS GOSWITZ, Special Training Division staff.

June 16: Qualitative identification of the chromosomes of malignant cells with ^{3}H-autoradiography—ISAO YAMANE, professor of microbiology, Research Institute, Tohoku University, Kitayobancho, Sendai, Japan.

June 23: The effect of oxygen and carbon dioxide on proteinase biosynthesis by *Streptococcus faecalis* var. *liquifaciens*—RONALD E. HARTMAN, summer research participant.

June 30: Splenic contraction and the optical density of blood—DAVID F. OPDYKE, summer research participant.